CHANGES IN LEG AND JOINT COORDINATION DURING LOCOMOTOR ADAPTATION IN AMPUTEES AND ABLE-BODIED SUBJECTS

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CHANGES IN LEG AND JOINT COORDINATION DURING LOCOMOTOR ADAPTATION IN AMPUTEES AND ABLE-BODIED SUBJECTS

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This dissertation is dedicated to the memory of Dr. Peter Mente, my undergraduate research mentor at North Carolina State University. He was a great mentor and an even better teacher who we lost much too soon. I came into his lab as a biology major who knew nothing about biomechanics except for that I liked my statics class more than my biology classes. When I graduated 2 years later, I knew I wanted to spend my life studying biomechanics. When I finished my undergraduate degree, Dr. Mente had taught me everything I knew about biomechanics and most of what I knew about conducting good research. Nine years later, I still find myself going back to his lessons regularly in my research. In addition to research, he gave me valuable advice on courses, graduate school and careers, and was an incredible teacher, even though he had little to no professional incentive for any of that. The best advice he gave me was to take his biomechanics course, which was the rare class that was students' toughest and also their favorite. When I teach now, that course is the ideal to which I compare my courses. If I can teach half as well as Dr. Mente, I will do my students a great service. I doubt I am unique in holding such esteem for Dr. Mente, whose teaching inspired a countless number of students. He is greatly missed by the NC State community and this research is dedicated to his memory.

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SUMMARY

Activities of daily life require humans to locomote in unfamiliar environments. We respond to these new environments through adaptation, a gradual change in movement parameters in response to a sensory error caused by altered environmental conditions. I investigated changes in coordination at the joint and leg level as subjects adapted to split-belt treadmill walking and altered visual feedback in hopping. As subjects adapted to increase leg force, they preferentially reduced deviations in joint torque that affected leg force. Once peak leg force reached a steady level, subjects reduced all joint torque deviations, regardless of relevance to leg force, suggesting that when subjects achieved the task goal, they switched from a minimal intervention strategy to a total noise reduction strategy. As subjects adapt to split-belt walking, they reduce hip work and shift to doing more ankle work in the step-to-step transition. Because ankle work in the step-to-step transition is more efficient, this ankle timing strategy likely contributes to the reduction in metabolic power during split-belt walking. Both amputees and controls gradually adapted step length symmetry in split-belt walking, demonstrating an aftereffect when the split-belt condition was removed. This result is consistent with previous studies of intact subjects and indicates that interlimb coordination is changed using feedforward control. Subjects also adapt to split-belt walking by moving farther backward in single support on the fast belt and less backward on the slow belt. This center of mass displacement strategy persists in amputees and controls, when the split-belt condition is introduced gradually or suddenly, and no matter which belt the prosthetic foot is on. This work suggests that mechanical changes that improve efficiency underlie the reduction in metabolic power during split-belt walking adaptation.

CHAPTER 1

INTRODUCTION

1.1 Motivation

Locomotion is central to human life. From an evolutionary perspective, our ancestors needed to be able to move from one location to another in order to evade predators, find mates and catch food. Today, locomotion is still essential to many activities of daily living. Locomotion requires few degrees of freedom, and humans have many more degrees of freedom than the minimum necessary to move. Before even considering the dozens of muscles in each leg, each leg has 3 primary joints – hip, knee and ankle – which provide more degrees of freedom than needed to walk or run. This means that humans need to be able to coordinate the two legs and joints within each leg such that their movements can combine harmoniously to result in forward movement.

Additionally, activities of daily living frequently require humans to locomote in new, unfamiliar environments. For example, walking from a paved sidewalk to grass or transitioning from running on wet, packed sand to running on loose, dry sand both present changes in surface friction and stiffness to which the body must adjust. These environmental changes alter sensory feedback, which can result in changes in motor behavior that occur gradually over time or more quickly. Gradual, non-permanent change in a motor parameter in response to a sensory error caused by altered environmental conditions is known as motor adaptation (Martin et al. 1996; Krakauer, Mazzoni, 2011). Adaptation is important because it makes movements more flexible in response to environmental changes (Bastian, 2008), but repeated adaptation can also lead to sustained motor learning (Reisman, Bastian, Morton, 2010, Reisman et al. 2013). Therefore, adaptation gives a glimpse into long-term motor learning processes such as those occurring during rehabilitation, but also allows for experiments that can be run in a more timely and controlled manner.

One population that can benefit from rehabilitation is trans-tibial amputees. In 2005, there were 1.6 million people with amputations in the United States alone, a number that is expected to more than double by 2050 (Ziegler-Graham et al. 2008). The second most common type of amputation in the United States is trans-tibial amputation, which removes the bottom portion of the tibia and fibula as well as the ankle and foot. Lacking an ankle leads to many gait impairments for trans-tibial amputees: they have higher metabolic cost of walking when compared to intact subjects (Houdijk et al. 2009), less propulsive force and impulse from their amputated side (Baker, Hewison, 1990; Silverman et al. 2008), shorter stance times on their prosthesis (Breakey, 1976), and increased incidence of osteoarthritis on their intact side (Morgenroth et al. 2011; Norvell et al. 2005), which likely results from overuse of the intact leg to compensate for the limited function of the prosthetic leg. While use of a powered prosthetic ankle can mitigate deficiencies in metabolic cost and ankle work (Herr, Grabowski, 2012), these devices are still prohibitively expensive, so most trans-tibial amputees continue to use passive prostheses, which release less than half of the energy normally generated by intact triceps surae muscles (Zmitrewicz, Neptune, Sasaki, 2007).

Trans-tibial amputees also have limited adaptability to new environments and step length asymmetry (Houdijk et al. 2012). These impairments make trans-tibial amputees an intriguing group to study using split-belt treadmill walking. The split-belt treadmill is a device in which two, side-by-side treadmill belts can move at different speeds. It is often used to study locomotor adaptation and can correct step length asymmetries in clinical populations with step length asymmetry (Finley, Bastian, Gottschall, 2013; Malone, Bastian, 2010; Malone, Bastian, 2014; Malone, Bastian, 2016; Mawase et al. 2013; Reisman, Block, Bastian, 2005; Reisman et al. 2013). Stroke survivors who return to symmetry after splitbelt walking do not quickly revert back to their asymmetric baseline behavior (Tyrell, Helm, Reisman, 2015), and amputees that improve propulsive ground reaction force symmetry in response to visual feedback show small but significant

reductions in metabolic cost (Davis et al. 2004), suggesting that the legs may be coordinated to achieve symmetry, Also, improving kinematic asymmetry is a commonly assumed clinical goal (Hassid et al. 1997). However, locomotor adaptation studies often focus on measures of kinematic interlimb coordination such as step length symmetry (e.g. Tyrell, Helm, Reisman, 2015; Reisman, Block, Bastian, 2005; Malone, Batian, 2014, Roemmich et al. 2014a) and double support times (Reisman, Block, Bastian, 2005), without focusing on kinetic variables, particularly at the joint-level. Joint-level kinetic impairments are particularly important. For trans-tibial amputees, as they have lost some inter-joint coordination due to their lack of a functional ankle (Toney and Chang, 2016). Finally, uncontrolled manifold (UCM) analysis, a method often employed to investigate interlimb and inter-joint coordination (Auyang, Chang 2013; Yen, Chang, 2010; Gorniak, Zatsiorsky, Latash, 2007; Scholz, Schoner, 1999; Yang, Scholz, Latash, 2007; Tseng, Scholz, Schoner, 2002), is normally best suited for steady state motor activities. Its reliance on variance calculated over many movement iterations makes it ill-suited for studying changes in coordination during adaptation.

The purpose of this dissertation is to better understand and quantify changes in interlimb and inter-joint coordination during intact and impaired locomotor adaptation. In pursuit of this purpose, I addressed three specific aims. Aim 1 established that healthy subjects selectively decrease task-relevant deviations in joint torque during adaptation of peak ground reaction force (GRF) in one-legged hopping. To accomplish this aim, I developed a modified UCM analysis that, for the first time, allowed for measuring deviations of individual hops in task space. In aim 2, I determined that healthy control subjects alter inter-joint coordination during split-belt walking adaptation by increasing ankle work done during the step-to-step transition and decreasing hip work. I also compared kinetic adaptations in trans-tibial amputees with healthy controls. In aim 3, I used gradual onset split-belt walking to show that split-belt walking adaptation changes inter-leg coordination in both healthy controls and trans-tibial amputees.

1.2 Optimal Feedback Control: Co-ordination of Local Variables to Accomplish a Task

Walking and hopping are fairly simple tasks mechanically, but, because multiple muscles, joints and limbs need to be coordinated to accomplish these tasks, they are complex in terms of motor control. Despite this redundancy, humans still locomote in a repeatable, consistent manner even while displaying considerable variability in the local variables that contribute to the locomotion task. This phenomenon can be explained in the framework of optimal feedback control theory using the minimal intervention principle (Todorov, Jordan 2002), which states that the motor control system favors correcting deviations in movement that affect task performance (i.e., task-relevant errors). Deviations that do not affect task performance are not corrected, because doing so would be energetically expensive. Minimization of energy and related variables in motor control is often described by cost functions. Cost functions typically include terms for error and energy (or a more easily measured correlate of energy such as muscle activation or mechanical work), which must be minimized for accurate, efficient task completion (e.g. Anderson, Pandy, 2001; Kuo, 1995; Emken et al. 2007; Shimansky, 2000; Shimansky, Kang, He, 2004).

Minimal intervention is supported by several lines of evidence, including multiple reaching and grasping studies (Liu, Todorov, 2007; Schlerf, Ivry 2011; Nguyen, Dingwell 2012). For instance, variance in muscle tension that changed accuracy of a fingertip force task was reduced compared to variance, which did not affect fingertip force (Valero-Cuevas et al. 2009). The idea that the nervous system preferentially corrects deviations that affect task performance is supported by animal studies, which show that limb-level dynamics are represented in the mammalian central nervous system (Bosco et al. 2006; Poppele et al. 2002) and maintained when peripheral nerve injury directly limits a specific joint (Chang et al. 2009; Bauman, Chang, 2013). This

combination of mathematical and direct physiological evidence suggests that minimal intervention generally explains how the nervous system coordinates movement.

Similar results were found in studies of motor control from the perspective of UCM analysis, which transforms variance into a task space and assesses task-relevant and task-irrelevant variance of local variables (e.g. joint angles) with respect to a task variable (e.g. endpoint displacement). UCM analysis demonstrates that task-irrelevant variance is larger than task-relevant variance for a wide array of tasks, including finger forces (Gorniak, Zatsiorsky, Latash, 2007), sit-to-stand transitions (Scholz, Schoner, 1999), and reaching (Tseng,, Scholz, Schoner 2002). While UCM analysis has been used to study adaptation of reaching movement, it is limited by focusing on variance (Yang, Scholz, Latash, 2007), which must be computed over a number of movement repetitions. This limitation obscures changes in task-relevant and task-irrelevant deviations in individual movements, which change over the course of several repetitions during learning processes.

UCM analysis has also been applied to walking and hopping (Black et al. 2007; Verrel et al. 2012; Rosenblatt et al. 2014; Auyang and Chang 2013; Toney and Chang 2013; Dingwell and Cusumano 2010). For example, subjects preferentially reduce task-relevant variance of leg segment angles to produce consistent medial lateral foot position during swing phase (Rosenblatt et al. 2014). Additionally, subjects reduce task-relevant joint angle and joint torque variance during hopping to maintain consistent leg length and orientation (Auyang, Yen, Chang, 2009), and to maintain consistent peak leg force (Yen, Auyang, Chang. 2009), respectively. Inter-leg coordination in walking follows a similar pattern, as variance in each leg's force is lower if it affects net vertical force of the two legs together (Toney, Chang, 2013). Additionally, ankle and knee torques covary to stabilize trailing leg force during walking (Toney, Chang, 2016).

1.3 Normal Walking Dynamics

Normal walking, which I define as walking with both legs moving at the same average speed, has been described physically as an inverted pendulum (Cavagna, Margaria,1966; Kuo, 2007). During single support, the center of mass (CoM) moves through an inverted pendular arc that requires no input of mechanical energy but simply transfers energy between gravitational potential energy and kinetic energy (Cavagna, Kaneko, 1977). This model has limitations, however. First, it only models a single step. Secondly, given that pendular motion requires no energetic input, the inverted pendulum model does not explain why constant speed walking has any metabolic cost greater than that of resting metabolism (Donelan, Kram, Kuo, 2002a; Kuo, Donelan, Ruina, 2005). These limitations are addressed through the principles of dynamic walking, which considers step-to-step transitions (STS) between the pendular arcs of each step (Kuo, 2007). The energetic cost of walking comes largely from this STS, during which the CoM velocity must be redirected from one pendular arc to the next (Kuo, Donelan, Ruina, 2005; Ruina, Bertram, Srinivasan, 2005). The work to accomplish this redirection is provided by the trailing leg (primarily the ankle), which must overcome negative work of the leading leg at heel strike in order to maintain forward velocity (Kuo, Donelan, Ruina, 2005). Dynamic walking models calculate mechanical work that correlates strongly with metabolic cost and accurately predicts that both quantities change with the fourth order of step length (Donelan, Kram, Kuo, 2002a). This indicates that work of the trailing leg during STS is a major determinant of overall metabolic cost in normal walking (Kuo, Donelan, Ruina, 2005). While dynamic walking models make many assumptions, such as rigid legs, they accurately predict experimental results and produce similar results to more complex models that have knees and trunks (McGeer, 1990).

Humans do much of their mechanical work during STS, likely because it is more efficient to do so. Human walking seems to be optimized for lowest metabolic cost, with preferred step lengths, widths and frequencies that have the highest efficiencies (Donelan,

Kram, Kuo, 2001; Donelan, Kram, Kuo, 2002b; Bertram, Ruina, 2001).Also, many models of walking based on energy minimization simulate human walking reasonably accurately (Minetti, Alexander, 1997; Anderson, Pandy, 2001; Emken et al. 2007). Kuo demonstrates that walking is most efficient when using propulsive work at the ankle of the trailing leg just before heel strike (2002). In contrast, using the hip for forward propulsion is 4 times as costly energetically. This hip work occurs primarily during single support, but, more recently, STS is has been defined by as beginning and ending at the minimum and maximum vertical CoM velocities, which agrees better with models of dynamic walking and actually extends STS into a brief portion of single support (Adamczyk, Kuo, 2009). Using these bounds of STS means that the remaining portion of single support is defined by inverted pendular motion of the CoM, so I will henceforth refer to this part of the gait cycle as pendular phase. Although it is less efficient, hip work is sometimes used by healthy individuals when work from the ankle is not sufficient. For example, at faster walking speeds, or when accelerating, the trailing limb cannot produce enough propulsive forces to compensate for increased energy loss at heel strike (Park, Park, 2013; Oh, Baek, Park, 2012). In these cases, subjects increase propulsion by the hip during single support, despite its poorer efficiency. In general, however, joint work is coordinated to maximize trailing ankle work in STS and minimize pendular phase work in order to improve energetic efficiency.

1.4 Dynamics of Walking with Trans-tibial Amputation

Because gait is most efficient when driven by propulsion from the trailing leg angle during STS, this presents a problem for trans-tibial amputees. Trans-tibial amputees have limited propulsion from the prosthetic trailing leg during STS (Bateni, Olney, 2002; Silverman et al. 2008; Zmitrewicz, Neptune, Sasaki, 2007; Houdijk et al. 2009; Adamczyk, Kuo, 2015). Amputees produce much less power from the ankle of a dynamic response prosthetic foot during late stance (Bateni, Olney, 2002), achieving less than half

the mechanical energy and less than an eighth of the power generated by intact triceps surae muscles (Zmitrewicz, Neptune, Sasaki, 2007). This results in lower propulsive work and impulse from the amputated limb (Adamczyk, Kuo, 2015; Silverman et al. 2008) and higher collisional energy loss at the sound leading limb (Houdijk et al. 2009). The intact limb must increase propulsive impulse and positive mechanical work to compensate for both of these deficiencies, but it compensate inefficiently way. Amputees increase intact leg work during pendular phase, and have higher metabolic costs than intact subjects (Hsu et al. 2005; Houdijk et al. 2009), a deficiency that worsens as speed increases (Torburn et al. 1995). While dynamic response prostheses store and return some energy, giving amputees lower metabolic cost than SACH feet (Wezenberg et al. 2014), they still do not allow amputees to walk as efficiently as those with powered prosthetic ankles or intact subjects (Herr, Grabowski, 2012).

Modeling trans-tibial amputation as a reduction in push-off work from one leg results in changes in CoM kinematics that match those observed experimentally, suggesting that kinematic asymmetries could be caused by the lack of propulsion from the amputated side (Adamczyk, Kuo, 2015). Trans-tibial amputees display a number of kinematic asymmetries, including shorter stance times on their amputated side (Breakey, 1976) and longer steps with their prosthetic leg leading than with their intact leg leading (Isakov et al. 1997). Amputees also have higher incidences of osteoarthritis, primarily on the intact side (Morgenroth et al. 2011, Norvell et al. 2005; Melzer, Yekutiel, Sukenik, 2001) but also in the hip on the amputated side (Kulkarni et al. 1998). Incidence of osteoarthritis in the intact knee has been related to joint loading (Baliunas et al. 2002; Foroughi, Smith, Vanwanseele, 2009) and, by extension, ground reaction force (Morgenroth et al. 2011), suggesting that osteoarthritis results from over-reliance on the intact side, but no clear, causal links between kinetic or kinematic gait asymmetries and osteoarthritis have been established.

1.5 Dynamics of Split-belt Treadmill Walking Adaptation

Adaptation is a gradual, non-permanent change in a motor parameter in response to a sensory error caused by altered environmental conditions (Martin et al. 1996). Adaptation is characterized by a change in a movement parameter rather than a change in movements (e.g. from walk to run) and by aftereffects (Bastian, 2008). When the perturbation that caused the initial adaptation is removed, subjects experience aftereffects – errors in the opposite directions that washout over time, with subjects eventually returning to baseline behavior (Shadmehr, Mussa-Ivaldi, 1994). These aftereffects and the gradual nature of adaptive changes are indicative of feedforward control (Kagerer, Contreras-Vidal, Stelmach, 1997; Savin, Tseng, Morton, 2010). Feedforward control involves a computational element in the nervous system that predicts effects of motor commands (Franklin, Wolpert, 2011), and is, therefore, often referred to as predictive control (Ogawa et al. 2014, Toney, 2016). In contrast, feedback control relies on reflex pathways to update motor commands nearly immediately based on afferent feedback of the perturbation (Lam, Anderschitz, Dietz, 2006; Nielsen, Sinkjaer 2002). This is also known as reactive control (Ogawa et al. 2014). Notably, in response to a sensory perturbation, some muscles can respond with behavior indicative of feedforward control while others react to sensory feedback immediately (Lam, Anderschitz, Dietz, 2006). Additionally, feedforward control also relies on sensory feedback from prior repetitions to correct for movement errors. Presumably, this occurs by updating gain of an internal model of the movement to account for environmental perturbations (Kawato, 1999; Kawato, Furukawa, Suzuki, 1987). Thus, there is an aftereffect when the perturbation is removed, because the internal model has been updated to account for the perturbation. The distinction between feedforward and feedback control is that feedback control relies solely on feedback to change the movement, and this change occurs much more quickly than in feedforward control. Cerebellar lesions impair feedforward control in locomotor

adaptation (Morton, Bastian, 2006), indicating that the cerebellum plays a critical role in feedforward control.

The most common way to study locomotor adaptation is through use of a split-belt treadmill, in which each foot steps on a separate treadmill belt and one belt moves faster than the other. Subjects initially respond to this perturbation with much larger step lengths with the slow leg leading, but they adapt over several minutes and correct this asymmetry, only to experience the opposite asymmetry when the belts return to moving at the same speed (Reisman, Block, Bastian, 2005). Subjects exhibit similar responses, which indicate feedforward control, in their double support times (Reisman, Block, Bastian, 2005; Patrick et al. 2014), ground reaction forces (Ogawa et al. 2014, Mawase et al. 2013), and leg angle phasing (Malone, Bastian, 2014; Reisman, Block, Bastian, 2005). As subjects adapted to split-belt walking, anterior braking force at heel strike (Ogawa et al. 2014) and vertical ground reaction force (Mawase et al. 2013) of the leg on the fast belt increase. In contrast, cost of transport and activity of lower limb muscles (tibialis anterior, gastrocnemius, vastus lateralis and biceps femoris) decreased as subjects adapted to the split-belt condition (Finley, Bastian, Gottschall, 2013). In this case, however, no aftereffect was noted when the split-belt condition was removed.

Other parameters change immediately after exposure to the split-belt condition due to feedback control. For example, while braking forces change gradually under feedforward control, propulsive ground reaction forces from the trailing leg during double support change immediately when split-belt walking is introduced (Ogawa et al. 2014). Additionally, stride lengths – calculated as anterior-posterior distance traveled by an ankle marker during ipsilateral stance – and individual limb stance times change immediately in split-belt walking (Reisman, Block, Bastian, 2005). In each of these cases, subjects switched immediately back to baseline behavior when the split-belt condition was removed. This lack of aftereffect suggests that changes in these motor

outputs were controlled by sensory feedback, without supraspinal inputs contributing to the change in control.

Feedforward adaptation of step length symmetry is a particularly consistent result of split-belt walking that has been replicated in children (Patrick et al. 2014), young and old adults (Malone, Bastian, 2016), and multiple clinical populations (Reisman et al. 2007, 2009, 2013; Tyrell, Helm, Reisman, 2014; Tyrell, Helm, Reisman, 2015; Roemmich et al. 2014a, 2014b). Step length symmetry has both spatial contributions (foot placement) and temporal contributions (interlimb timing), which are adapted separately in split-belt walking (Finley et al. 2015; Malone, Bastian, 2010). The spatial component of step length is due to the flexion of the "lead limb" between ipsilateral toe off and heel strike. The temporal component is caused by the backward distance moved by the contralateral leg in stance on the treadmill. The temporal component can be broken into velocity and time-dependent components, which are not independent from one another. Together, these form step length, which is measured as the anterior-posterior distance between the leading and trailing ankle at heel strike. Changes in step length symmetry during adaptation are caused by equal changes in both step time and step position at a 2:1 belt speed ratio, although step position (the spatial component) has a larger impact on step length asymmetry at a 3:1 belt speed ratio (Finley et al. 2015).

Split-belt treadmills can perturb gait by moving belts in opposite directions. This creates hybrid walking with one leg stepping forward and the contralateral leg stepping backward (Choi, Bastian, 2007). Adaptation of step lengths to this condition does not transfer between legs, nor do adaptations transfer between conditions – from backward stepping to forward stepping or vice versa. However, transfer of adaptation between less disparate types of walking (i.e. treadmill and overground walking) does occur, particularly when the split-belt condition is introduced gradually (Roemmich, Bastian, 2015; Torres-Oviedo, Bastian, 2012).

Split-belt walking also has the potential to correct asymmetries in clinical populations. If subjects start with a baseline step length asymmetry, putting the foot that takes longer steps on the slow belt initially exacerbates the asymmetry, but then the asymmetry is corrected in the aftereffect. This is known as error augmentation therapy (Malone, Bastian, 2014; Reisman, Bastian, Morton, 2010). Split-belt adaptation has been shown to correct baseline step length asymmetries in stroke survivors (Malone, Bastian, 2014; Reisman et al. 2007; Reisman et al. 2009; Tyrell, Helm, Reisman, 2014; Tyrell, Helm, Reisman, 2015; Finley et al. 2015) and Parkinson's disease patients (Roemmich et al. 2014a, 2014b). The theory behind error augmentation is that, after repeated exposures to split-belt walking, the aftereffect in step length symmetry will cease to wash out and patients will walk more symmetrically (Reisman, Bastian, Morton, 2010). However, the aftereffect only persists for about half of stroke survivors 3 months after a 4-week split-belt treadmill walking intervention (Reisman et al. 2013). Stroke survivors with the largest baseline step length asymmetries were most likely to show sustained improvements in step length symmetry after the intervention, perhaps because patients with smaller baseline asymmetries had the opposite asymmetry in the aftereffect, and symmetric aftereffects are less likely to wash out (Tyrell, Helm, Reisman, 2015).

While split-belt adaptation is primarily studied through sudden onset of the split-belt condition, this condition can also be introduced by accelerating one belt gradually. In reaching, aftereffects wash out more slowly when perturbations in visual feedback are introduced gradually rather than abruptly (Kagerer, Contreras-Vidal, Stelmach, 1997), but this result does not extend to gradually introduced split-belt walking (Torres-Oviedo, Bastian, 2012; Roemmich, Bastian, 2015; Patrick et al. 2014), which has similar aftereffects and washout to sudden onset split-belt walking. However, aftereffects after gradual onset split-belt walking do transfer to overground walking better than sudden onset split-belt aftereffects (Torres-Oviedo, Bastian, 2012). This suggests that, when perturbations produce smaller errors, the nervous system attributes these errors to body

movements rather than the context of walking on a treadmill. Furthermore, gradual onset split-belt walking presents less of a challenge to balance than sudden onset, especially on the slow belt (Sawers and Hahn, 2013, Sawers et al. 2013). This is of particular importance for split-belt studies which place an impaired leg, which may have more difficulty with balance, on the slow belt. Therefore, gradual onset split-belt walking may have greater potential for clinical application than sudden onset split-belt walking.

In both reaching and split-belt walking adaptation, subjects reduce metabolic power as they adapt (Finley, Bastian, Gottschall, 2013; Huang, Ahmed, 2012)**.** This reduction of metabolic power was suggested to be driving split-belt adaptation, but the mechanism behind it is not well understood. Recent work indicates that the reduction in metabolic power in adaptation correlates with a shift from doing propulsive leg work primarily during pendular phase to primarily doing propulsive work by the trailing in STS (Thajchayapong et al. in preparation). However, the changes in kinetics at the joint-level during split-belt adaptation are unknown. Compared to leg work, joint-level mechanics are a more direct measure of muscle work (Donelan, Kram, Kuo, 2002b) and are thus an important part of any mechanism explaining the reduction in metabolic power as subjects adapt to split-belt walking.

1.6 Objective and Aims

The primary objective of this dissertation is to investigate changes in coordination of joints and of legs during locomotor adaptation. I pursued this objective through completing three specific aims. The first aim used a hopping task to investigate changes in joint coordination when the goal of the task was explicitly stated and the error away from this goal was made clear via visual feedback. The second and third aims focused on leg and joint coordination during split-belt treadmill walking, in which the gait task was implicit, meaning subjects would potentially be able to optimize multiple costs without

explicit instructions constraining them to prioritize one cost such as minimizing task error.

1.6.1 Aim 1: To establish whether task-relevant deviations selectively decrease during adaptation of peak GRF in single-legged hopping.

I developed a modified UCM analysis method that quantifies task-relevant and task-irrelevant deviations for every hop cycle and used this method to quantify reduction of task-relevant deviations as subjects adapt to higher peak GRF demands provided by visual feedback. Consistent with MIP, I hypothesized that subjects would reduce task-relevant deviations in joint torques more than irrelevant deviations during adaptation. Once subjects were no longer reducing peak GRF error, I expected them to begin reducing total torque deviations regardless of task-relevance. The results of Aim 1 showed how joint torque coordination changes during adaptation to increased GRF in one-legged hopping, illustrating the extent to which MIP applies to locomotor adaptation.

1.6.2 Aim 2: To determine how joint work changes as intact and trans-tibial amputee subjects adapt to split-belt walking and explore amputees' biomechanical compensation mechanisms

Metabolic power decreases as subjects adapt to split-belt walking, but the joint-level mechanism behind this improved efficiency is unknown. I hypothesized that controls would have high hip work at the onset of split-belt treadmill walking, but would reduce this hip work and increase STS work done by the trailing leg ankle on the fast belt as they adapted. I proposed this switch from hip work to trailing ankle work as a joint-level biomechanical mechanism for the reduction in metabolic power during split-belt walking adaptation. I further hypothesized that amputees would be unable to utilize this mechanism of increasing the fast (prosthetic) leg ankle work but would instead rely on work from their intact leg on the slow belt for propulsion.

1.6.3 Aim 3: To test whether split-belt treadmill walking would change amputees' baseline inter-leg coordination in post-adaptation and investigate related changes in work and CoM movement

Trans-tibial amputees may reduce their step length asymmetries in response to split-belt walking, but changes in amputees' mechanics after split-belt walking are unknown. My primary hypothesis was that, after gradual onset split-belt walking with their prosthetic leg on the slow belt, amputees would have step length symmetry that was more positive in early post-adaptation than in the slow baseline trial. I further hypothesized that, compared to baseline, both amputees and controls would adapt to gradual split-belt walking by move further backward during fast leg single support and less backward during slow leg single support in late adaptation – the same CoM displacement strategy subjects used in the sudden onset split-belt walking. Lastly, I hypothesized that, when fast (intact) leg step length increased in early post-adaptation, work in inefficient phases of the gait cycle, such as pendular phase, would increase.

CHAPTER II

AIM 1: LOCOMOTOR CONTROL SWITCHES FROM MINIMAL INTERVENTION PRINCIPLE IN EARLY ADAPTATION TO NOISE REDUCTION IN LATE ADAPTATION

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2.1 Introduction

The human body possesses more degrees of freedom than are necessary to complete any given motor task. Despite this redundancy, humans still manage to perform tasks in a repeatable and consistent way even while exhibiting considerable variability in the manner with which they accomplish these tasks. This phenomenon has been explained within the framework of optimal feedback control theory using the minimal intervention principle (Todorov and Jordan 2002), which states that the nervous system preferentially corrects deviations in movement that have a negative effect on performance (i.e., task-relevant errors). The rationale is that correcting deviations requires energy and is not worth the energetic cost unless it directly leads to improved performance. Findings from a number of reaching and grasping studies support minimal intervention as a general principle that explains how the nervous system organizes movement (Valero-Cuevas et al. 2009; Liu and Todorov 2007; Schlerf and Ivry 2011; Nguyen and Dingwell 2012). For example, variance in muscle tension relevant to altering a fingertip force task is lower than the task-irrelevant variance, which has no effect on fingertip force (Valero-Cuevas et al. 2009). Similarly, studies from the perspective of uncontrolled manifold (UCM) analysis distinguish the task-relevant and task-irrelevant variance of local variables (e.g., joint angles) when this variance is transformed into the task space of a hypothesized control parameter (e.g., end-point position). In a range of motor tasks including sit-to-stand transitions (Scholz and Schoner 1999), reaching (Tseng et al. 2002), finger forces (Gorniak et al. 2007) and locomotion (Black et al. 2007; Verrel et al.

2012; Auyang and Chang 2013; Toney and Chang 2013; Dingwell and Cusumano 2010), task-irrelevant variance of the local variables contributing to performance has been shown to be larger than variance that negatively affects the task performance (i.e., task-relevant). This suggests that the nervous system selectively reduces variations in local variables (e.g., joint dynamics) that affect the task (e.g. limb dynamics). This inference, however, has been made largely by examining the variance structure that accumulates over numerous, successive repetitions of a consistently performed task rather than over the course of a changing adaptive response.

The adjustments in task-relevant and task-irrelevant deviations in local variables that occur on an iterative basis, particularly during the process of locomotor adaptation, have not been thoroughly examined. Understanding how joint dynamics adapt within a task-space would provide insight into whether the nervous system utilizes minimal intervention principle to control and adapt locomotor performance. In our usage, adaptation occurs in response to an error signal and consists of a change in a movement parameter (e.g. limb end-point force) that progresses over many repetitions rather than fully correcting for the perceived error immediately (Martin et al. 1996). Because of the dynamic nature of adaptation, it is advantageous to consider the task-relevance of deviation structures for individual repetitions rather than a single variance computed across the entire adaptation. The error signal to induce adaptation can be generated by visuomotor perturbation or through a direct perturbation on the performance. A visuomotor perturbation consists of the alteration of an otherwise accurate visual representation of the subject's performance without the subject's knowledge. For example, perturbations of visual feedback on hand position during a reaching task (Mazzoni and Krakauer 2006) or on step length during walking (Kim and Krebs 2012) cause subjects to adapt their movements to counteract the perceived perturbation. In locomotor adaptation induced by a split-belt treadmill walking task, subjects adapt to the direct perturbation of walking on two belts moving at different velocities by reducing both the induced step length asymmetry (Reisman et al. 2005) and metabolic cost (Finley, Bastian, Gottschall, 2013). Subjects also exploit redundancy between the local variables stride length and stride time to maintain constant speed during steady-state treadmill walking (Dingwell et al. 2010). Locomotor adaptation research has typically focused on

the changes occurring in limb-level or interlimb parameters like stride length, stride time and ground reaction force (Finley, Bastian, Gottschall, 2013; Dingwell et al. 2010; Torres-Oviedo and Bastian 2010; Vasudevan and Bastian 2010; Dingwell et al. 1996). These global changes have a direct bearing on locomotor performance and must often be modified according to the experimental paradigm. Limb-level dynamics are represented in the mammalian central nervous system (Bosco et al. 2006; Poppele et al. 2002) and maintained even when peripheral nerve injury directly limits a specific joint (Chang et al. 2009; Bauman and Chang 2013), indicating that whole limb function likely represents an important level in the hierarchical organization of sensorimotor control (Loeb et al. 1999).

Our approach here, however, is to focus on a different level of the sensorimotor control hierarchy and study joint torques as local variables that directly impact limb function. Joint torques result, in part, from combined muscle forces acting across a joint and, thus, serve as a good proxy for combined muscle actions. Additionally, how the coordination of joint torques in a limb-force-equivalent task space affects limb force can be determined analytically and quantitatively through use of a Jacobian matrix (Yen et al. 2009; Yen and Chang 2010). Alternatively, we could measure muscle activation patterns with electromyography, and there is evidence that muscle activations are coordinated to achieve limb-level function (McKay and Ting 2008, Chvatal et al. 2011). Our approach to study deviation structure in joint torques provides a complementary method for studying what we believe is a similar level of the control hierarchy. As there is no direct way to quantitatively relate muscle activity to limb force output, however, our approach allows us to more directly relate the effects of muscle action (i.e., joint torque) to limb function (i.e., force) without relying on experimental correlations that relate muscle activity to limb force. Joint-level variables are coordinated to produce stable, consistent leg angles during hopping (Auyang et al. 2009), consistent center of mass position during walking and standing up from a seated position (Verrel et al. 2012; Scholz and Schoner 1999), and consistent limb-level force output in hopping, running and walking (Yen et al. 2009; Yen and Chang 2010; Yen 2011; Toney and Chang 2013). Examining how cycle-by-cycle deviations in joint torques are structured with respect to a limb force task space and how this structure changes over time would provide a means to better understand

how the nervous system may utilize hierarchical organization to control limb force during human locomotor adaptation.

Variance (or deviation) structure of joint-level variables in task space, however, has not been previously studied during locomotor adaptation. Currently, there is no consensus as to a general framework for motor adaptation among the few studies that have investigated local variable changes with respect to task space during upper extremity movements. After practicing a reaching task, subjects showed greater decreases in task-irrelevant variance compared to task-relevant variance, which was contrary to minimal intervention principle (Domkin et al. 2002). Conversely, in agreement with a minimal intervention principle, Kang and colleagues (2004) found that subjects were able to produce a consistent net force across four fingers by reducing their task-relevant variance. Similarly, when subjects adapted to reaching in a force field, they preferentially reduced task-relevant variance in joint angles throughout the adaptation paradigm (Yang et al. 2007). The discrepancy between these motor adaptation studies may have been caused by quantifying the structure of variance over many repetitions across the entire motor adaptation process (Domkin et al. 2002; Yang et al. 2007; Kang et al. 2004). Although the uncontrolled manifold approach (Scholz and Schoner 1999) is appropriate when applied to steady state behaviors, a preferable method would be quantifying deviation structure of each repetition separately. This is because variance structure calculated across a number of repetitions may not provide the temporal resolution necessary to capture rapid adaptive changes that can occur over only a few repetitions. This is especially true when relatively large changes occur very early in adaptation followed by a long period of steady performance.

In human locomotion, joint torques are co-varied with respect to a limb force equivalent task space to maintain a consistent limb force output during hopping, running, and walking gaits (Yen et al. 2009; Yen and Chang 2010; Yen 2011; Toney and Chang 2013). Moreover, the biomechanics of both hopping and running is accurately modeled by considering the net actions of the leg to act like a linear spring (Farley et al. 1991; Farley and Gonzalez, 1996), a phenomenon observed across a wide variety of species (Full and Koditschek, 1999; Cavagna et al. 1977). Together, this suggests the joints are coordinated to achieve consistent, spring-like behavior from one hop to the next through

consistent limb force production and indicates that hopping can be a tractable model to study the control of running (Blickhan 1989, McMahon and Cheng 1990; Ferris and Farley 1997). Furthermore, because the mechanics are relatively simple and well understood, hopping and running provide an appropriate limb control schema that can be used to test the analytical techniques developed for this manuscript. In steady state hopping, variance in joint function (i.e., torques and angles) across many hops is biased to minimize only those joint deviations that tend to cause a deviation in the performance task (i.e., peak force on the ground and limb kinematics, respectively; Yen et al. 2009; Yen and Chang 2010; Auyang et al. 2009; Auyang and Chang 2013). The way in which this coordination changes from hop to hop during locomotor adaptation, however, is unknown and would provide evidence for what control strategies may be accessed during locomotor adaptation. Therefore, our approach here is to give subjects an explicit task to match a fixed visual target representing a previously identified implicit task goal of hopping, peak GRF. In particular, we focus on the changes in coordination of the local variables (i.e., joint torques) redundant to this limb-level force task when we implement a shift to the visual feedback unbeknownst to the subject. Our goal is to test whether these joint-level torque changes during locomotor adaptation occur with respect to a task space representing limb force. This would suggest the nervous system references a task space representation of limb dynamics when regulating joint dynamics during locomotor adaptation. Furthermore, the relative changes of task-relevant and task-irrelevant joint torque deviations will reveal whether these changes that are local to the global task variable of limb force adhere to a minimal intervention control principle.

Specifically, we determine whether hop-by-hop task-relevant deviations in joint torques selectively decrease when subjects adapt peak vertical ground reaction force (GRF) to a visuomotor perturbation task during single-legged hopping. Since large changes can occur over only a few hop cycles during early adaptation, we used a modified UCM analysis method that allowed us to calculate task-irrelevant and task-relevant deviations in joint torques for each individual hop cycle during locomotor adaptation. Our primary purpose in this study was to investigate how joint torques change in task space while subjects were required to increase peak GRF in response to a visuomotor perturbation. Subjects had a fixed visual target representing peak GRF, which

would compel them to explicitly reduce task-relevant joint torque deviations to increase limb force and accomplish this visual matching task. Importantly, however, no such restriction was placed on task-irrelevant joint torque deviations, which by definition do not affect achievement of the peak force needed to match the visual target. Therefore, consistent with the minimal intervention principle, we hypothesized that subjects would reduce task-irrelevant deviations in joint torques less than task-relevant deviations as they adapted to the shifted visual feedback to produce higher peak limb forces.

Additionally, we posed two secondary hypotheses that the adaptation of limb force would exhibit a gradual reduction of GRF error at the beginning of each successive shifted feedback trial; and that limb force output would display negative aftereffects when the visuomotor perturbation was removed. These results would suggest that, rather than solely correcting errors in limb force based on visual feedback errors in the previous few hops, adaptation during hopping involves using feedback to update an internal model, which is then referenced for feedforward control of limb force. Feedforward control is consistent with previous results in reaching adaptation (Kagerer et al. 1997; Izawa et al. 2008) and gait adaptation (Savin et al. 2010). Thus, limb force errors suggesting a feedforward control strategy would indicate that subjects are undergoing locomotor adaptation rather than simply correcting GRF errors based solely on feedback from hop to hop.

2.2 Methods

2.2.1 Experimental design

Eleven healthy subjects (5 male) with means (±SD) of 25.5±3.7 years of age, 66.8±7.2 kg body weight, 177.3±9.8cm height and 92.7±4.7cm right leg length participated in this study. All subjects gave written, informed consent prior to participating in the study in accordance with an approved protocol granted by the Georgia Institute of Technology human subjects Institutional Review Board. Subjects were excluded if they had a history of neuromuscular injuries, severe leg injuries requiring surgery or any leg injury 3 months prior to participating in the study. Subjects had no prior knowledge of the purpose of the study.

Each subject completed 11, 30-second trials, hopping on their right leg to a metronome beating at 2.2Hz, which resulted in approximately 66 hops per trial. Subjects were given at least 2.5 minutes of rest between trials. All 30-second trials were grouped into one of four blocks representing the different visual feedback conditions. Each block contained multiple trials. In the baseline block, subjects completed 2 trials with no visual feedback. The average peak GRF from these trials was used to determine the target given as visual feedback in subsequent blocks of trials. Peak vertical ground reaction force (GRF) was chosen as the target, because previous research indicates that maintaining peak GRF is a goal in hopping (Yen et al. 2009; Yen and Chang 2010). Next, subjects completed a block of 2 trials while viewing real-time visual feedback of their current peak GRF in comparison to the visual target, which was the average peak GRF determined in the baseline block. Visual feedback was given using a custom Labview program (National Instruments, Austin, TX, USA) and consisted of two vertical bar graphs displayed on a large monitor (110cm x 62cm dimensions) ~3m in front of the subjects at eye level. One vertical bar provided a visual representation of the target GRF and did not change for the entirety of the experiment. The other vertical bar gave visual feedback of peak vertical GRF from the current hop and changed with each hop (figure 2.1A). Subjects were instructed to match the height of the vertical bar representing the peak force that they exerted on the floor to the height of the target vertical bar. This was the only instruction concerning visual feedback that the subjects received. The first trial of the non-shifted feedback block was used to allow subjects to acclimate to accurate visual feedback, and the second trial was used for comparison to subsequent trials. The next block consisted of four trials where the visual feedback was inaccurate due to a baseline shift. Subjects were not made aware of the shift in the visual feedback.

During the shifted feedback block, subjects were given visual feedback of peak GRF that was reduced by an amount equal to 10% of the baseline target GRF. This shift was applied to the visual feedback vertical bar rather than the target column, so subjects were only asked to match a single, unchanging target over the course of the study. Based on pilot studies, 10% of peak GRF was chosen to be high enough to be outside of normal variation in peak GRF, but low enough that subjects could reach it while maintaining a hopping frequency of 2.2Hz. This induced subjects to adapt to this visuomotor

perturbation by increasing peak GRF to match the visual target. This 10% shift represented a substantial amount of force increase. As the baseline peak GRF averaged 2.43 body weights (BW), this 10% visual shift resulted in an average increased peak vertical GRF of 24% BW. After the shifted feedback block of four trials, the visuomotor perturbation was removed without their knowledge and subjects completed an additional block of three post-shift trials in which there was no shift in visual feedback. For the shifted feedback and post-shift blocks, subjects were considered to have reached their goal behavior when peak GRF reached a steady state.

To control for the effect of visual feedback alone, without any shift, a subset of 8 subjects returned several months after the initial experiment to complete an extended control experiment consisting of 2 baseline trials and 6 non-shifted feedback trials. Based on a power analysis (GPower 3.1,Heinrich Heine University, Dusseldorf, Germany, see Faul et al 2009), this extended control experiment could detect effect sizes similar to those observed in the primary experiment with a power of 0.8. Consistent task-relevant deviations across these additional four non-shifted feedback trials would indicate that changes during the original shifted feedback condition were due to the shift in visual feedback rather than simply the presence of visual feedback.

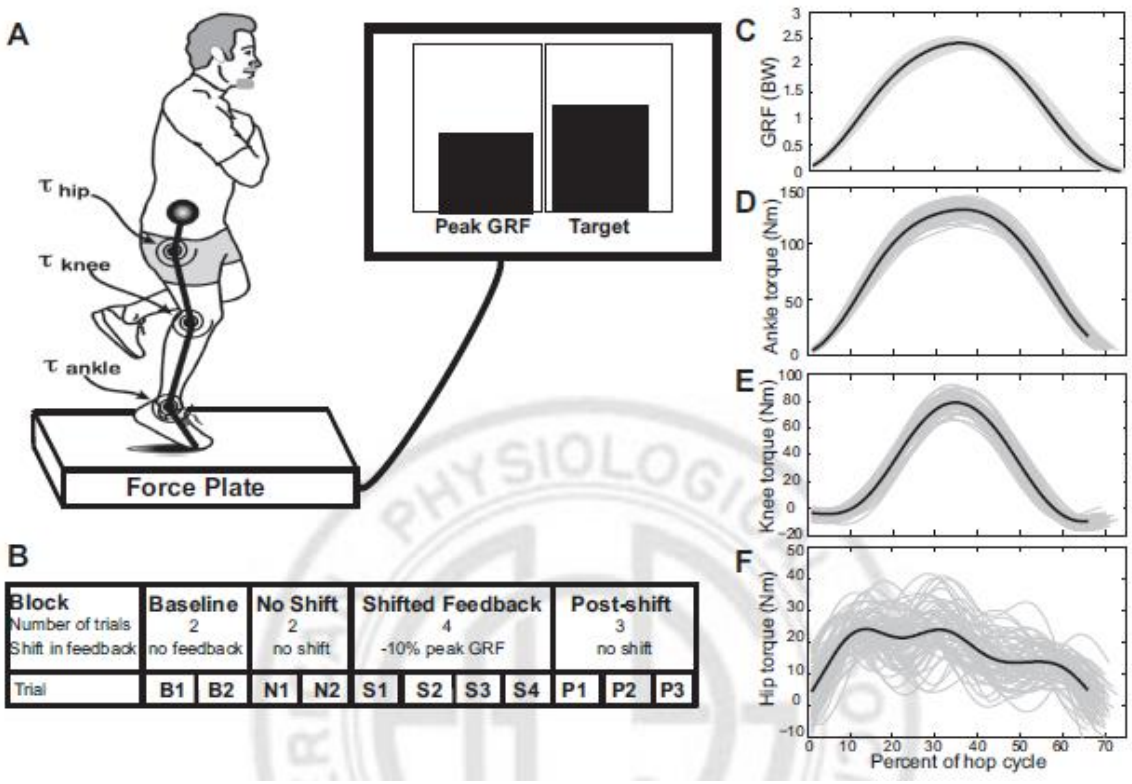

Figure 2.1: A. Experimental Setup: During non-shifted, shifted and post-shift blocks, subjects received visual feedback of a constant target GRF and the peak GRF of each hop. The scale of each plot was from 0-5 bodyweights, although this scale was not visible to the subject. B. Experimental Protocol. The top row contains the name of the block condition, number of trials in the block, and the shift in visual feedback of the peak GRF vertical bar on the left of the screen. The bottom row gives abbreviations for each trial that will be used in subsequent figures. C-F. Ground reaction force and ankle, knee and hip torques for a control trial of a representative subject (average of all hops in trial in black, individual hops in gray).

2.2.2 Data collection and processing

We placed 16 reflective markers on lower body, anatomical landmarks (second metatarsal phalangeal joint, calcaneus, lateral malleolus, shank, lateral femoral epicondyle, thigh, anterior superior iliac spine and posterior superior iliac spine) of each subject. We tracked sagittal plane locations of ankle, knee and hip joint centers using a six-camera motion analysis system (120Hz, Vicon, Los Angeles, CA, USA), and collected GRFs with a force plate (1,080Hz, AMTI, Watertown, MA, USA). Both force and camera data were low-pass filtered at 10Hz using a fourth order Butterworth filter. A custom Matlab (Mathworks, Natick, MA, USA) program was used to compute joint

angles and joint torques as previously described (Auyang et al. 2009; Yen et al. 2009). We defined a hop cycle as the time between initial foot contacts with the ground in consecutive hops and defined stance phase as the phase of each hop cycle when the measured GRF was greater than 32N. Data were time normalized so that each hop cycle had 100 data points, similar to gait cycles used in walking studies.

2.2.3 Data analysis

The GRF error for non-shifted, shifted and post-shifted trials was calculated as the difference between the visual target and the representation of peak vertical GRF given by visual feedback. For each hop cycle, we determined the time when highest peak vertical GRF occurred. To find peak GRF error, GRF error was averaged over 5% of the hop cycle centered about the peak GRF time. Although we analyzed data over the entire hop cycle, our main focus was on changes in peak GRF and joint torques at the time of peak GRF. This is precisely the time in the hop cycle when subjects reduce task-relevant variance of joint torques during steady-state hopping (Yen et al, 2009). We calculated a Jacobian relating changes in joint torques to changes in vertical GRF similarly to a previously described method (Yen et al. 2009). Sagittal plane torques from the hip, knee and ankle joints were included in our analysis. Previous uncontrolled manifold analyses used joint angles averaged over the entire trial as reference angles to calculate this Jacobian that estimates the manifold. This assumes that the average over the trial is the desired behavior. Since performance changes throughout adaptation, the trial average is not as appropriate a point of reference during our shifted feedback trials. Rather, the steady state behaviors reached at the end of the non-shifted, shifted and post-shifted blocks are more representative of the goal motor behavior for each block. Therefore, we averaged across the last 30 hops from each of the non-shifted, shifted and post-shifted block of trials to find the reference posture ($\vec{\theta}^{r}$) for each block, which was used to calculate the Jacobian for that respective block. T-tests confirmed that peak GRF in the last 30 hops of each block were consistent with the last 40 and last 50 hops of their respective blocks ($p \geq 0.29$), indicating that this was a steady-state reference posture. In this way, we were assured that the GRF had reached a steady, consistent value. To validate the linearity of the system, we used the derived Jacobian and the measured joint torques to calculate an estimate of the measured vertical GRF using a previously

described method (Yen et al. 2009). For all subjects and hops, the estimated GRF calculated from the Jacobian was very similar to the experimentally measured vertical GRF. Across all subjects and trials, the average slope of the regression comparing measured and calculated was very close to unity (0.94) and the lowest R^2 value for any single hop was 0.95 (see figure 2.1A), indicating that the assumption of a linear manifold is valid. We then used the Jacobian (S) to find the null space ($\vec{\varepsilon}$) for every 1% of time of each hop cycle (equation 1).

$$0 = S(\vec{\theta}^r) \cdot \vec{\varepsilon} \qquad (1)$$

By projecting differences between joint torques (X) at each 1% of the hop cycle and reference torques (X^r) into the null space of the Jacobian (S), we could determine the component of a single joint torque deviation that was parallel to the manifold ($X_{\parallel}$, equation 2). As with our reference posture, reference torques were also averaged from the last 30 hops of each block of trials.

$$\vec{X}_{\parallel} = \sum_{i=1}^{n-d} \vec{\varepsilon}_i^{\,T} (\vec{X} - \vec{X}^r) \vec{\varepsilon}_i \qquad (2)$$

Where n = 3 is the number of local degrees of freedom (i.e., joint torques) and d=1 is the number of global degrees of freedom (i.e., limb force). The remaining torque deviations ($X_{\perp}$) are orthogonal to the manifold (equation 3).

$$\vec{X}_{\perp} = (\vec{X} - \vec{X}^r) - \vec{X}_{\parallel} \qquad (3)$$

The variables $X_{\parallel}$ and $X_{\perp}$ are calculated in the same manner as motor-equivalent and non-motor-equivalent joint deviation vector in a previous study (Mattos et al. 2011). Normalizing $X_{\parallel}$ and $X_{\perp}$ by the square root of degrees of freedom gave us cycle-specific task-irrelevant and task-relevant deviations, respectively (equations 4 and 5).

$$\text{task-irrelevant deviations} = \vec{X}_{\parallel} / \sqrt{(n-d)} \qquad (4)$$

$$\text{task-relevant deviations} = \vec{X}_{\perp} / \sqrt{d} \qquad (5)$$

Here we used single cycle projections in the null space instead of projections of variance over many locomotor cycles as we have done previously to study steady-state walking and hopping (Toney and Chang 2013; Yen and Chang, 2010). This allowed us to distinguish the task relevance of a single joint torque deviation within a single hop cycle and to track how this deviation changed over successive hops, which can occur rapidly

during early adaptation. During our steady-state baseline trials, squaring the task-relevant and task-irrelevant deviations calculated with our modified uncontrolled manifold analysis and averaging these results across all hops in the trial to find variance yielded similar results to the non-goal equivalent and goal equivalent variance metrics we have previously used to analyze steady-state data (figure 2.2B and 2.2C). In other words, during steady state hopping our cycle-by-cycle modified uncontrolled manifold analysis agrees with the traditional uncontrolled manifold approach we have used in previous steady-state studies.

Mean values of task-relevant and task-irrelevant deviations are biased toward subjects with high variability in joint torques. That is, a subject with higher overall variability in torques would have both larger task-relevant and task-irrelevant deviations, meaning her data may be overrepresented when averaging deviations across subjects. Therefore, we calculated a single-cycle index of deviation structure (SCIDS) to compare the normalized ability to structure joint torque deviations in task space across subjects (equation 6).

SCIDS = (task-irrelevant deviations – task-relevant deviations)/($\|\vec{X} - \vec{X}^r\|/\sqrt{n}$) (6)

where $\|\vec{X} - \vec{X}^r\|/\sqrt{n}$ is the magnitude of total torque deviations – a measure of total joint torque variation regardless of task-relevance. SCIDS is a normalized difference between single-cycle task-relevant and task-irrelevant deviations. A positive SCIDS value indicates that the task-irrelevant deviation is larger than the task-relevant deviation for that hop. An increase in the SCIDS value from the beginning to the end of adaptation would support the hypothesis that subjects selectively decrease task-relevant torque deviations more than they decrease task-irrelevant deviations over the course of adaptation, which is consistent with a minimal intervention principle. Although UCM analysis of single repetitions has been previously used to study finger force deviations projected into task space (Scholz et al. 2003), the Jacobian used in that analysis relied on the assumption that the pattern of force-sharing between fingers doesn't change over the time of each repetition. While this assumption holds for finger forces (Zatsiorsky et al. 2000), the SCIDS analysis employed here is more appropriate for locomotion, because

postural changes within each cycle alter the relative influences of different joints on vertical GRF and require recalculation of a new Jacobian for each time point in the hop cycle.

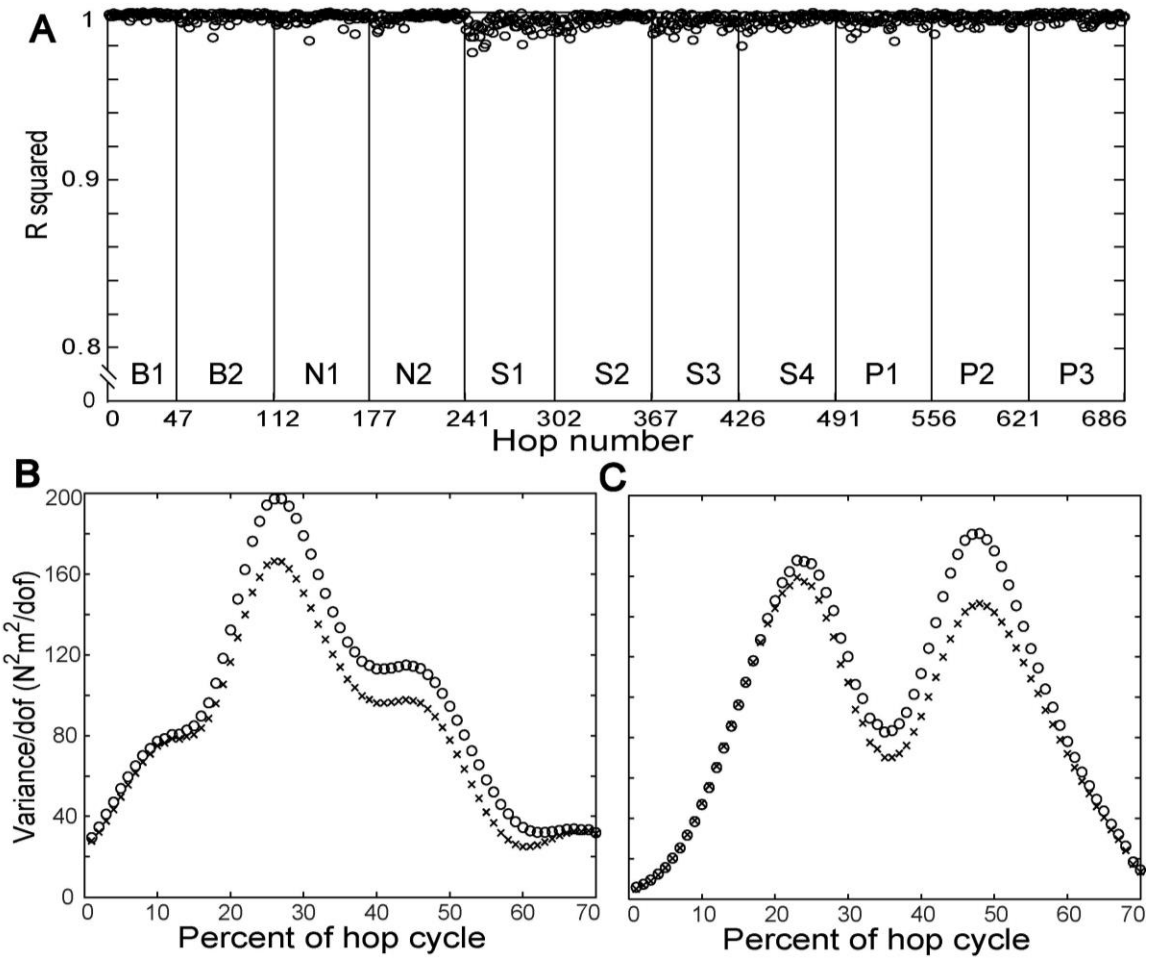

Figure 2.2: Validation of the single cycle modified UCM method. A. R^2 values of the relationship between endpoint forces calculated from the Jacobian S and experimental vertical GRF data for each hop of a representative subject. B. In steady-state hopping, task-irrelevant deviations squared and averaged across all hops in the trial (open circles) are equal to goal equivalent variance (x's) for the second baseline trial of a representative subject. C. Similarly, task-relevant deviations squared and averaged across all hops in the trial (open circles) are equal to non-goal equivalent variance (x's) for the same trial.

In summary, the single-cycle analysis methods used here differed from previous analyses because we calculated the Jacobian from steady-state behavior at the end of each

block of trials rather than computing a single variance across a number of repetitions during which the performance changes. The end of each block represented a period during each condition when subjects were no longer altering their peak GRF performance. Thus, our current method has the advantage of allowing us to track task-relevant and irrelevant torque deviations of individual hops with respect to a task space defined by a functional goal of hopping (i.e., limb force). This greater temporal resolution is better suited for describing rapid changes that often occur in early adaptation.

2.2.4 Statistical analysis

All data are reported as means (±standard errors) across subjects unless otherwise indicated. We used one-tailed, paired t-tests (alpha = 0.05) to compare the mean of the first 10 and last 10 hops of each trial for peak GRF error, task-relevant deviation, task-irrelevant deviation, magnitude of total torque deviation and SCIDS (SPSS, IBM, Armonk, NY, USA). Instead of comparing one hop to another, we primarily used means of the first and last 10 hops, which were computed for each subject before averaging across subjects, because we wanted to specifically assess differences between the beginning and end of each trial without results being skewed by one errant hop. To assess changes across adaptation and de-adaptation blocks, we also used paired t-tests to compare the first and last 10 hops of each block of trials and performed Bonferroni corrections for all t-tests involving the first or last 10 hops of each block of trials (e.g. first 10 hops of S1 and last 10 hops of S4), where multiple tests were necessary.

Bonferroni corrections were made by multiplying the p-values obtained by the number of t-tests conducted, allowing us to use a consistent definition of statistical significance ($\alpha = 0.05$) throughout the study. For example, the first 10 hops of the first post-shift trial (P1) were compared the last 10 hops of that trial (P1) and also to the last 10 hops of the last post-shift trial (P3), so a Bonferroni correction was used for both of these tests. Rather than changing the alpha value to 0.025, we doubled the calculated p-values, which is equivalent for determining significance but simplifies reporting our results by maintaining the same alpha value (0.05) for all tests. Standard errors were computed by dividing standard deviations calculated across subjects by the square root of the number of subjects. Data from the beginning and end of each trial, which were

compared with t-tests, had similar variance and were normally distributed, indicating that parametric tests were appropriate.

2.3 Results

As expected, all subjects displayed an adaptation of peak GRF when visual feedback was shifted to explicitly require greater peak limb forces. During the first three shifted feedback trials, subjects significantly reduced the magnitude of error in peak GRF from the beginning to the end of each respective trial (figure 2.3). There was a 54% decrease in GRF error between the first 10 hops of the first shifted feedback trial (S1) and the first 10 hops of the final shifted feedback trial (S4, $p<0.01$). Similarly, the peak GRF error of the very first hop of S1 was significantly larger than that of the first hop of S4 ($p<0.001$). In the first post-shifted feedback trial, GRF error initially exhibited a negative aftereffect but corrected to near zero error by the end of this trial, representing an 82% decrease in error magnitude ($p<0.02$). For both shifted and post-shifted feedback blocks, GRF error remained unchanged within later trials (late adaptation and late post adaptation, respectively). Data from each subject followed the same trends exemplified by the group. During the first trial of the non-shifted feedback block, GRF error exhibited a decreasing trend ($p<0.07$), but the second non-shifted feedback trial showed no changes in GRF error.

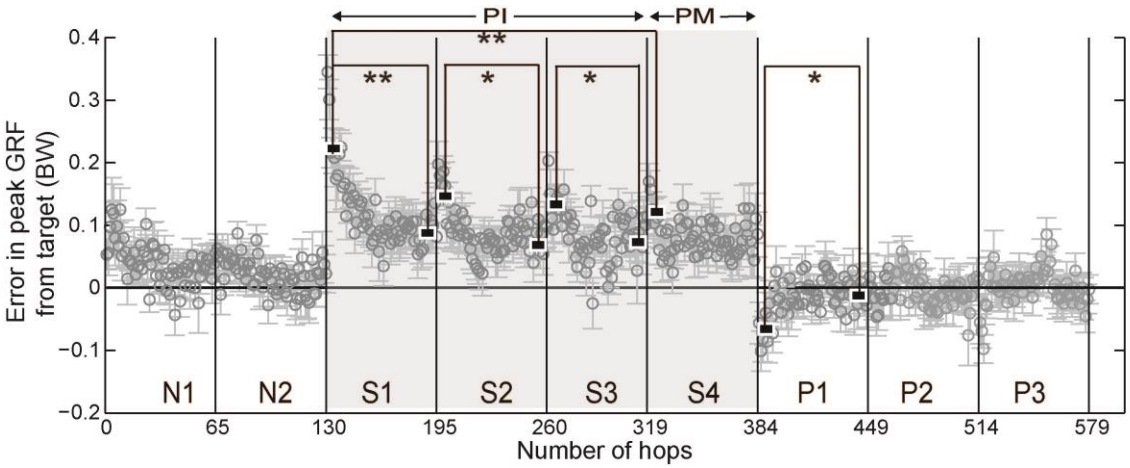

Figure 2.3: Magnitude of error between peak GRF and target over time. GRF error decreases in first 3 shifted feedback trials, the performance improvement (PI) phase, and is unchanged in the final trial, the performance maintenance (PM) phase. Peak GRF error magnitude also decreased in the first post-shift trial. Symbols are means ± standard errors across all 11 subjects. Brackets indicate significant difference between averages of first 10 and last 10 hops, as well as first ten hops of S1 compared to first ten hops and last 10 hops of S4 (* indicates $p<0.05$, ** indicates $p<0.01$).

Task-relevant joint torque deviations generally mirrored the changes observed in peak GRF as anticipated. Task-relevant deviations significantly decreased during the first, second and last shifted feedback trials, as well as the first post-shift trial ($p<0.05$, figure 2.4A). Interestingly, we did not observe any similar concurrent changes in the average magnitudes of individual joint torques. The decrease in task-relevant deviations between the first 10 hops of the shifted feedback block and the first 10 hops of the final shifted feedback trial was highly significant ($p<0.01$). While peak GRF error showed a decreasing trend only in the first non-shifted trial, task-relevant deviations exhibited significant decreases during two of the other non-shifted trials ($p<0.05$, figure 2.4A). In the extended control experiment when subjects only experienced non-shifted visual feedback, within trial reductions in task-relevant deviations were significant for only the first of the six non-shifted feedback trial ($p<0.03$) (figure 2.4C).

In contrast, task-irrelevant joint torque deviations did not mirror the pattern of GRF errors. Task-irrelevant torque deviations did not change early in the shifted feedback block and decreased only at the end of this block in the last trial ($p<0.02$, figure 2.4B). Task-irrelevant deviations also decreased significantly in the first and last post-

shifted trial ($p<0.05$), and exhibited a decreasing trend in the second post-shifted trial ($p=0.08$, figure 2.4B). During the extended control experiment, task-irrelevant deviations displayed a small but significant decrease in the third non-shifted feedback trial ($p<0.03$). This represented a 14% decrease over the trial, which was the smallest measured significant change in torque deviations across all conditions studied. For comparison, the average variation of task-irrelevant deviations during all non-shifted trials of the extended control experiment was 11%.

As a result of the task-specific changes in the components of joint torque deviation, a clear structure of joint torque deviations projected into the force equivalent task space emerged during adaptation. Our metric for the normalized difference between task-irrelevant and task-relevant deviations, SCIDS, significantly increased within the first and second shifted feedback trials indicating an ever-increasing alignment with the target limb force manifold ($p<0.01$ and $p<0.05$, respectively, figure 2.5). SCIDS remained positive and largely unchanged throughout the third and fourth shifted feedback trial and the entire post-shifted feedback block. SCIDS also increased during the first non-shifted feedback trial following the baseline condition suggesting an initial effect of visual feedback alone ($p<0.02$). Notably, we saw a general increase in SCIDS across the entire adaptation condition when comparing the first 10 hops and final 10 hops of the entire shifted feedback block ($p<0.01$). The increase in SCIDS between the first 10 hops of the first shifted feedback trial and the first 10 hops of the final shifted feedback trial also suggest that our subjects were improving their ability to quickly respond to the shift within each trial over the course of the adaptation period ($p<0.01$).

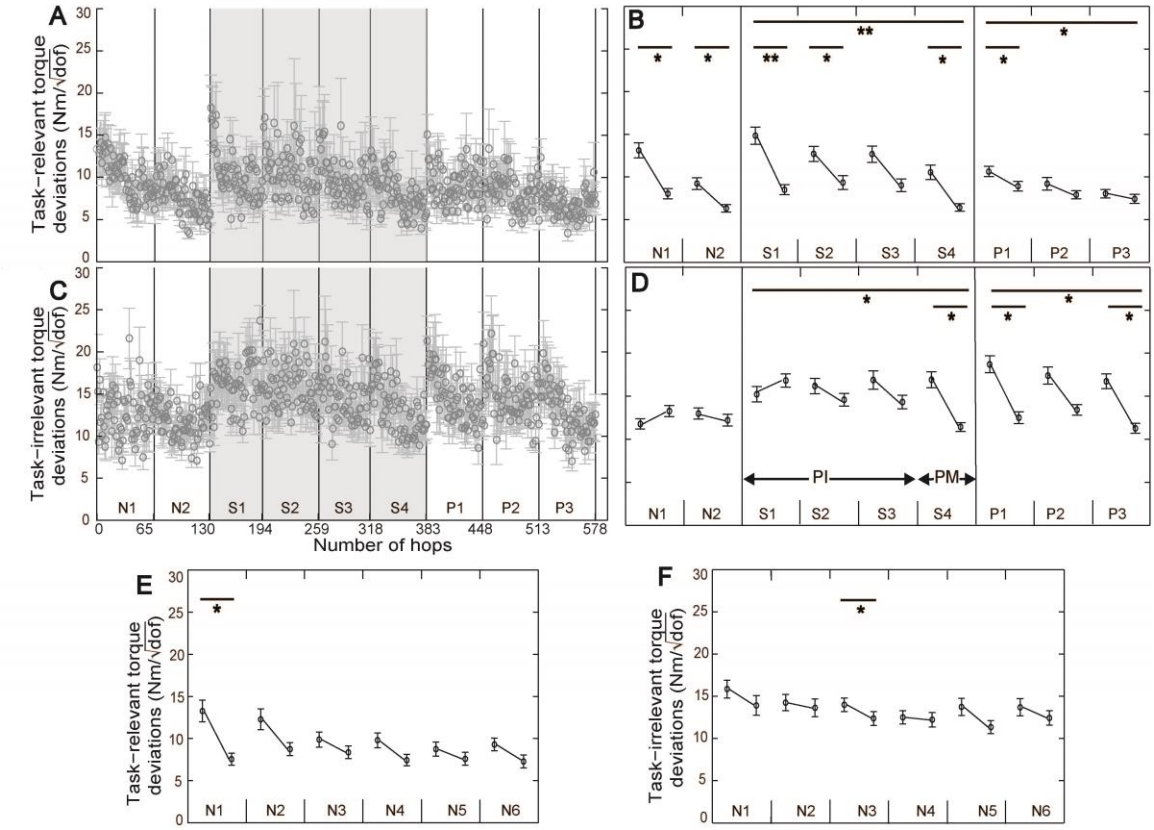

Figure 2.4: Task-relevant (A) and task-irrelevant (C) joint torque deviations for every hop, averaged across subjects in the primary experiment. Average task-relevant (B) and task-irrelevant (D) deviations for the first 10 and last 10 hops of each trial in the primary experiment. Average task-relevant (E) and task-irrelevant (F) deviations for the extended control experiment for the first 10 and last 10 hops of each trial. Data are means ± standard errors across 11 subjects. (* indicates $p<0.05$, ** indicates $p<0.01$, PI – performance improvement, PM – performance maintenance).

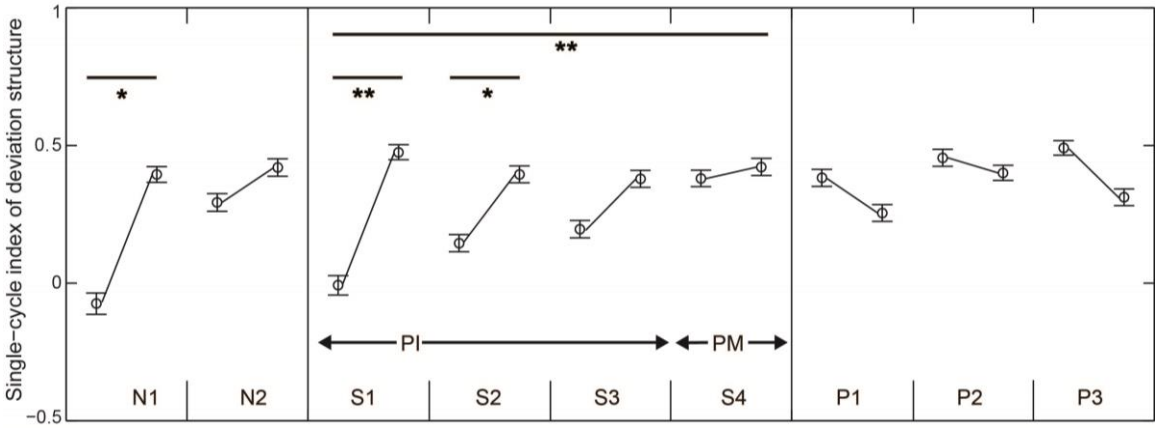

Figure 2.5: Single-cycle index of deviation structure (SCIDS), a measure of coordination of joint torques, across the first and last ten hops of each trial. Data are means ± standard errors across 11 subjects. (* indicates $p<0.05$, ** indicates $p<0.01$, PI – performance improvement, PM – performance maintenance).

The de-adaptation period during the post-shifted feedback trials appeared to be influenced by decreases in total torque deviations. While SCIDS did not change during the post-shift block, total torque deviations did significantly decrease within the first and last post-shifted feedback trial ($p<0.03$) and exhibited a decreasing trend in the second post-shifted feedback trial ($p<0.06$, figure 2.6). Overall, total torque deviations showed similar changes to task-irrelevant deviations. Total torque deviations were also significantly reduced within the fourth shifted feedback trial at the end of the adaptation period ($p<0.02$). We also observed significant decreases in total torque deviations within blocks across both the shifted and post-shifted feedback blocks ($p<0.01$).

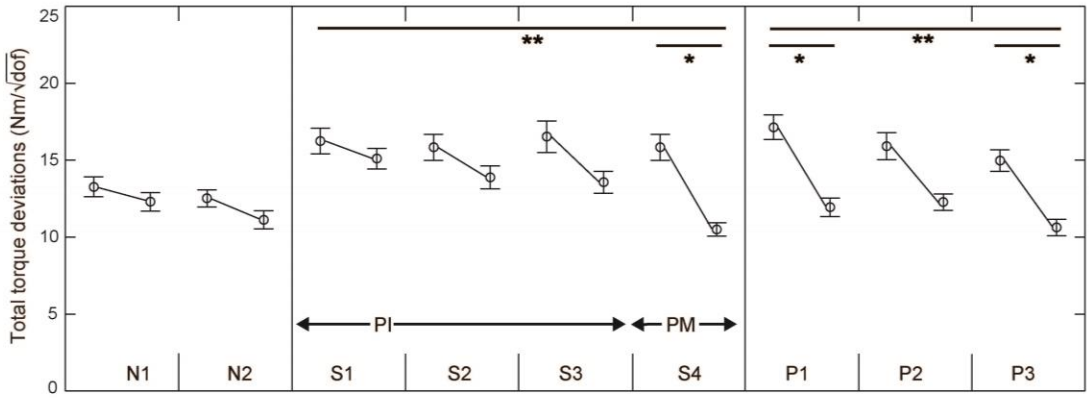

Figure 2.6: Total joint torque deviations across the first and last 10 hops of each trial. Data are means ± standard error across 11 subjects. (*indicates $p<0.05$, ** indicates $p<0.01$, PI – performance improvement, PM – performance maintenance).

2.4 Discussion

Subjects followed minimal intervention principle to adjust their joint dynamics during the performance improvement phase of the visual feedback of GRF matching task. When viewed in the task space of the target limb force, task-relevant joint torque deviations decreased more than task-irrelevant deviations during early adaptation, when the greatest decreases in GRF error took place. The shifted feedback block of trials can be further separated into a performance improvement phase when peak GRF error was decreasing (i.e., early adaptation) and a later performance maintenance phase when peak GRF error remained relatively unchanged (i.e., late adaptation). In this study, the first two shifted feedback trials and beginning of the third trial made up the performance improvement phase as evidenced by the progressively decreasing GRF errors, while the remainder of the shifted feedback block represented the performance maintenance phase (figure 2.3). During performance improvement, we saw a greater effort to align the torque deviation structure with the target force-equivalent manifold (i.e., as indicated by an increasing SCIDS metric). The increased deviation structure, SCIDS, was solely the result of a decrease in task-relevant joint torque deviations while task-irrelevant joint torque deviations remained unchanged. While task-relevant deviations must decrease to increase limb force due to the explicit task imposed by the visual target, it was not known *a priori* that task-irrelevant joint torque deviations would remain unchanged during

performance improvement. For example, a wholesale decrease in total joint torque deviations, with equal decreases in both task-relevant and task-irrelevant joint torque deviations irrespective of the target force manifold, could also have delivered improved performance in matching the visual target representing peak force. The increase in SCIDS during the performance improvement phase of adaptation is consistent with minimal intervention principle. The increase in SCIDS also clarifies previous studies of hopping under steady state conditions, in which joint torque variance that affects peak GRF (calculated across the entire trial) is lower than variance that does not affect peak GRF (Yen et al. 2009, Yen and Chang 2010). To our knowledge this is the first demonstration of minimal intervention principles during locomotion that shows a cycle-by-cycle preferential reduction in the local variables (i.e., joint torques) that determine limb-level task performance (i.e., peak GRF). Importantly, the task-irrelevant joint torque deviations were left unaltered. This suggests that the locomotor system likely references a representation of the limb force task space when controlling the motor output responsible for generating joint torques. Based on the performance improvement phase, locomotor adaptation in hopping follows minimal intervention principle by reducing only the task-relevant torque deviations while allowing task-irrelevant deviations to remain high.

The secondary hypotheses that ground reaction force error would decrease between the start of each shifted feedback trial followed by a negative aftereffect during the first post-shift trial was supported, suggesting that visuomotor adaptation of limb force is under feedforward control during hopping. Subjects responded to shifts in visual feedback by increasing peak GRF both within and across trials. Particularly, GRF error at the beginning of each shifted feedback trial progressively decreased compared to the prior trial. After 3 trials of shifted feedback, GRF error at the beginning of the final adaptation (S4) trial was significantly lower compared to the beginning of S1 even though the hop at the very beginning of the S4 trial does not have feedback from a previous hop (figure 2.3). If the reductions in peak vertical GRF were solely due to simple feedback error correction, we would expect GRF error at the beginning of the last shifted feedback trial (S4) to be equally as large as in the first hop of S1. Then GRF error would decrease across the S4 trial in response to errors in visual feedback. The first recorded hop in S4 occurs after at least 2.5 minutes of rest and without the benefit of

visual feedback from a previous hop, so attenuation of error in that first hop in S4 supports the hypothesis that a predictive control strategy is being used. Furthermore, GRF error did not decrease from the beginning to the end of the S4 trial. This result and the aftereffect we observed in P1 after the shift had been removed indicate that subjects were not using hop-to-hop error correction driven solely by feedback control. Instead, they were more likely predicting the required GRF in a feedforward manner. This feedforward control could possibly be achieved by referencing an internal model of the limb dynamics required to reach a GRF that matches the visual target. An internal model updated in response to visual feedback errors in trials S1, S2 and S3 could have produced the results seen in S4. Feedforward control is a fundamental feature of adaptation that is seen in other gait and reaching movements (Kagerer et al. 1997; Savin et al. 2010). Our results suggest that the locomotor adaptation of limb force during hopping in response to visual feedback is the result of a similar process.

We have taken a different approach to minimal intervention principle than previous studies, which often have redundancy built into the task performance (Schlerf and Ivry 2011; van Beers et al. 2012; Liu and Todorov 2007; Ranganathan and Newell 2010; Diedrichsen 2007). For example, when reaching for a linear target, subjects allow for more performance deviations in the task-irrelevant direction along the length of the target (Schlerf and Ivry 2011). Also, when force field perturbations occur early in targeted reaching, subject hand positions vary greatly until just before reaching the target, when hand position is most relevant to achieving the task (Liu and Todorov 2007). These approaches studied deviations occurring in the performance parameter (e.g., hand position) rather than the local variables that contribute to the performance parameter (e.g., joint angles). When the task does not have built-in redundancy, however, minimal intervention can still be observed in the organization and control of the redundant anatomical elements that contribute to task performance. For instance, when producing a target fingertip force, task-relevant variance in activity of redundant muscles is consistently lower than task-irrelevant variance (Valero-Cuevas et al. 2009). Here, we show that subjects adhere to a minimal intervention principle when organizing their joint dynamics to improve limb force performance during a hopping locomotion task.

An interesting result was that task-relevant deviations decreased not only in shifted feedback trials during adaptation but also in baseline trials with non-shifted feedback. This can also be observed in the SCIDS metric. When visual feedback is first introduced, SCIDS is negative due to relatively high task-relevant deviations. However, SCIDS quickly increases in the presence of visual feedback and is positive through the second baseline trial. These results indicate that visual feedback of any limb force target induces subjects to adopt a minimal intervention strategy even when there is no shift in visual feedback. The results of the *post hoc* extended control experiment, however, demonstrate that when subjects continue to hop with accurate visual feedback without the shift, task-relevant deviations quickly level off after the first trial with no substantial changes over the subsequent 5 trials (figure 2.4E). There was a small but significant decrease of 14% in task-irrelevant deviations in the third non-shifted feedback trial. This was small in comparison, however, as significant decreases in task-irrelevant deviations during the primary experiment with shifted visual feedback ranged between 48 and 50% and appeared consistently over the shifted feedback trials. If we consider any trial providing visual feedback on peak GRF error to be a task that requires performance improvement, then the brief performance improvement with non-shifted feedback actually supports the greater observation that minimal intervention principle is used when limb force errors are to be explicitly minimized. Therefore, it is likely that the more robust reductions in task-relevant deviations to reduce GRF error during limb force adaptation in the primary experiment can be attributed mostly to the heightened performance improvement demanded of the shift in feedback rather than the visual feedback alone.

During the performance maintenance phase, all joint torque deviations decreased simultaneously regardless of task relevance. This indicates that the limb force control strategy had switched from one of minimal intervention during performance improvement to a strategy of joint-level noise reduction during performance maintenance. We use the term noise reduction not to signify reducing noise in GRF performance but rather reduction of variability in the local variables, in this case joint torques (Müller and Sternad, 2004). Reducing noise at the joint level may have a functional significance beyond producing a limb force that matches the visual target more

accurately. As we observed, the reduction in total noise does not occur until after subjects had reached a steady state peak GRF error. Noise reduction, therefore, must be motivated by something other than the drive to improve limb force performance. A similar pattern is observed during adaptation to a three-finger force-balancing task (Latash et al. 2003). Whereas only task-relevant variance decreased early in finger force adaptation, task-irrelevant variance decreased after subjects had practiced enough to perform the task accurately. The decrease in task-irrelevant variance during performance maintenance may have been related to secondary task constraints besides the explicit task goal of generating force. That the switch from minimal intervention to noise reduction occurs during practice of activities as diverse as discrete finger force and rhythmic leg force generation suggests that it may originate from a centralized control strategy.

In our study of locomotor adaptation during hopping, we similarly suspect that subjects reduced all joint torque deviations during task maintenance in response to task constraints unrelated to GRF error. During treadmill walking, subjects preferentially correct deviations away from the manifold over short time scales, but also reduced task-irrelevant deviations over longer time scales to approach a preferred operating point that is based partly on energetic cost (Dingwell et al. 2010). This indicates that minimizing energetic cost is a secondary goal in locomotion compared to objectives more immediately related to performance. Similarly, reducing energetic cost may be the secondary task constraint causing decreases in task-irrelevant deviations during performance maintenance in hopping adaptation. Minimization of energy used by the muscles is implicated to underlie many movement control strategies. For example, energy minimization is an important component of the optimal feedback control theory of movement (Todorov 2004). The cost functions that best model reaching and object manipulation include minimizing energy or effort (Berret et al.2011; Nagengast et al. 2009). Minimization of energy or related quantities like muscle activity are also often used to accurately model human locomotion (Miller et al. 2012; Anderson and Pandy 2001; Emken et al. 2007). Recent experimental findings also support the importance of energy reduction during the process of motor adaptation in arm reaching (Huang et al. 2012) and split-belt treadmill walking (Finley, Bastian, Gottschall, 2013). Furthermore, a cost function that uses performance error alone fails to predict learning behavior in

adaptation, but a cost function using both performance error and energetics associated with muscle activations accurately predicts adaptation in both reaching and gait (Emken et al. 2007). The reduction in total joint torque deviations during task maintenance in the current study may result from gradually moving toward an optimal posture or set of muscle synergies (Chvatal and Ting 2011) that allows subjects to minimize energy while maintaining the same peak GRF performance. Future studies would be necessary to further investigate this possibility.

Subjects reduced peak GRF errors and task-relevant joint torque deviations early in the first post-shifted feedback trial, indicating that the performance improvement phase during de-adaptation occurred very rapidly. This was not surprising, as task errors are often corrected more quickly in de-adaptation than adaptation (Davidson and Wolpert 2004; Malone, Bastian, 2010; Bastian 2008), particularly when adaptation is caused by a sudden visuomotor perturbation (Kagerer et al. 1997). Faster de-adaptation can be further explained by a two-rate adaptation model, involving fast and slow adaptive processes that respond to sensory errors at different rates (Smith et al. 2006). In our subjects, while the fast adaptive process may have changed quickly in response to the errors created by shifted visual feedback during adaptation, the slow adaptive process would have been less receptive to these errors and remained biased toward the baseline peak GRF in the non-shifted feedback condition. When the shift in feedback was removed, the reliance on the slow adaptive process would explain the rapid return to the baseline peak GRF that we observed during the post-shift trials.

Such a quick reduction in peak GRF error means that for the remainder of the de-adaptation block, subjects should be in the performance maintenance phase, and this was the case. Task-irrelevant deviations significantly decreased or exhibited a decreasing trend in all post-shifted feedback trials while SCIDS remained positive and unchanged. This may be due to the relative familiarity and simplicity of the post-shifted trials, which has been observed in similarly simple bimanual reaching tasks (Domkin et al. 2002). Our subjects adapted to a relatively difficult task of generating an additional 10% (~160N) of peak GRF, which initially required a minimal intervention strategy. De-adaptation to a naturally preferred performance baseline, in contrast, is a relatively easy task and our subjects exhibited only a brief performance improvement phase.

In summary, we found that locomotor adaptation of limb force in response to a shifted visuomotor transformation does not result only from hop-to-hop error correction, but is more likely achieved by feedforward control. We applied a single-cycle analysis within the framework of the uncontrolled manifold approach to assess the time course of adaptation of joint torques projected into a task space relative to limb force. We conclude that there are two phases in the locomotor adaptation of limb force in hopping, which are characterized by two different control strategies. In the first phase of performance improvement, ground reaction force error is reduced through direct, preferential reduction of only the task-relevant deviations in joint torques and is consistent with the principle of minimal intervention. In the second phase of performance maintenance, all deviations in joint torques are significantly reduced regardless of their effect on ground reaction force. The change in control strategy occurs in locomotor adaptation with the duration of the performance improvement phase correlated with the difficulty of the task. These results from hopping may represent a more general control strategy that could be insightful for a better understanding of locomotor limb force adaptation during running and hopping gaits.

CHAPTER III

AIM 2: TWO BIOMECHANICAL STRATEGIES FOR LOCOMOTOR ADAPTATION TO SPLIT-BELT TREADMILL WALKING IN TRANS-TIBIAL AMPUTEES AND CONTROL SUBJECTS

3.1 Introduction

When humans walk continuously under novel conditions, the nervous system responds by gradually modifying locomotor control in response to ongoing sensory feedback. Locomotor adaptation can be characterized by a movement parameter that changes gradually over many repetitions in response to errors in sensory feedback caused by an altered environment (Martin et al. 1996; Bastian, 2008). Locomotor adaptation is also characterized by aftereffects, which linger when the environmental perturbation is removed. This process of locomotor adaptation and its aftereffects is commonly experienced when running on to hard pavement after having run on sand for a prolonged period. Because these aftereffects do not immediately dissipate when the perturbed sensory feedback is immediately removed, they considered to be indicative of predictive, feedforward control of movement (Ogawa et al. 2014; Kagerer, Contreras-Vidal, Stelmach, 1997).

Locomotor adaptation can be readily studied during split-belt treadmill walking, in which each foot is placed on a separate belt, as each belt moves at a different speed (Prokop et al. 1995; Jensen, Prokop, Dietz, 1998). Over the course of several minutes of split-belt walking, interlimb parameters such as symmetry between step lengths and percentage of the gait cycle in double support demonstrate adaptive changes (Reisman, Block, Bastian, 2005). Adaptation of step length symmetry is a robust finding, which has been replicated in stroke survivors (Reisman et al. 2007; Reisman et al. 2010), Parkinson's disease patients (Roemmich et al. 2014a; Roemmich et al. 2014b), and over a wide range of conditions in healthy subjects (Malone, Vasudevan, Bastian, 2011; Malone, Bastian, 2010; Torres-Oviedo, Bastian, 2012; Torres-Oviedo, Bastian, 2010, Finley, Statton, Bastian, 2014). During split-belt walking, vertical (Mawase et al. 2013) and braking (Ogawa et al. 2014) ground reaction forces (GRF) of both legs also exhibit feedforward, adaptive changes at initial contact, although vertical GRF in single support

and propulsive GRF exhibit immediate changes indicative of reactive feedback control. Furthermore, over the course of adaptation to split-belt walking, subjects reduce both leg muscle activity and metabolic power (Finley, Bastian, Gottschall, 2013).

Although we know that metabolic power decreases during split-belt walking adaptation, the changes in joint work that may be responsible for this improvement in walking economy are unknown. During overground walking, humans metabolic cost is determined largely by mechanical work in the step-to-step transition (STS), which is much more efficient than from the hip in single limb support (Donelan, Kram, Kuo, 2002a; Kuo, 2002). This result explains why metabolic cost is increased in trans-tibial amputees wearing a passive prosthesis that lacks the ability for active ankle torque (Houdijk et al. 2009; Adamczyk, Kuo, 2015) and in healthy subjects with immobilized ankles (Wutzke, Sawicki, Lewek, 2012). We also recently showed that, as mechanical power decreases during split-belt walking adaptation at a 3:1 belt speed ratio, healthy subjects decrease propulsive work during single support and increase work on the center of mass (CoM) from their trailing leg in STS (Thajchayapong et al. in preparation). However, changes in joint work during split-belt walking adaptation are still unknown. Furthermore, split-belt walking has not been tested on trans-tibial amputees. Because trans-tibial amputees have limited propulsion from their prosthetic ankle (Silverman et al. 2008; Crimin et al. 2014; Fey, Klute, Neptune, 2011), which typically provides the trailing leg power during STS, split-belt walking with the prosthesis on the fast belt is a useful model for studying compensation during locomotor adaptation.

The purpose of this study was two-fold: (1) to determine how joint work changes as subjects adapt to split-belt walking with one belt moving twice as fast as the other (2:1 ratio), and (2) to explore biomechanical compensation mechanisms that trans-tibial amputees use during split-belt walking to improve economy. We hypothesized that matched controls would have high hip work at the onset of split-belt treadmill walking, but would reduce this hip work and increase STS work done by the trailing leg ankle on the fast belt as they adapted. We propose this switch from hip work to trailing ankle work as a joint-level biomechanical mechanism for the reduction in metabolic power during split-belt walking adaptation. We further hypothesized that amputees would be unable to

utilize this mechanism of increasing the fast (prosthetic) leg ankle work and would instead rely on work from their intact leg on the slow belt for propulsion.

3.2 Methods

3.2.1 Subjects

Eight trans-tibial amputees (6 male, BW: 80.4±16.9kg, intact leg length; 92.0±6.4cm, 1 congenital, 7 traumatic) and eight matched control subjects with intact limbs (6 male, BW: 81.5±14.1kg, leg length: 91.8±4.7cm) participated in this study. Matched control subjects were not significantly different from amputees in leg length (mean difference = 0.025cm, $p=0.43$) or body mass (mean difference = 1.05kg, $p=0.25$). All subjects gave informed consent prior to the study in accordance with a protocol approved by the Georgia Institute of Technology Institutional Review Board. Amputees wore their own, custom-fit prostheses with dynamic response feet. All amputees had their prosthesis for at least 6 months prior to the study and were able to walk for 15 minutes without additional walking aid. Control subjects were matched to amputees in leg length, body weight (BW) and gender.

3.2.2 Experimental Protocol

We first determined preferred walking speed (PWS) for each subject as they walked at various treadmill speeds. Subjects started at 1.3m/s and speeds were varied by 0.1m/s increments. At each speed, subjects indicated if the speed was "too fast," "too slow" or "just right."

We then implemented our experimental protocol relative to each subject's PWS. The presentation of walking conditions was similar to several previous split-belt treadmill studies (Figure 3.1, Reisman, Block, Bastian, 2005; Ogawa et al. 2014). Subjects completed three 2-minute baseline trials walking with belts at the same speed (tied-belt at 75%, 150%, and 75% PWS), then walked for 15 minutes in a split-belt condition, with one belt moving at 150% PWS and one moving at 75% PWS. All amputees walked with the intact leg on the slow belt and amputated leg on the fast belt. For all trials, the leg moving at 150% PWS during adaptation will be called the fast leg, and the contralateral

leg will be called the slow leg. Lastly, subjects completed a 10-minute, post-adaptation trial in which both belts moved at 75% PWS. Subjects wore a safety harness throughout and held an anterior handrail for the first 30 seconds of each trial to prevent falls. A mirror allowed subjects to see their foot placement while maintaining forward gaze.

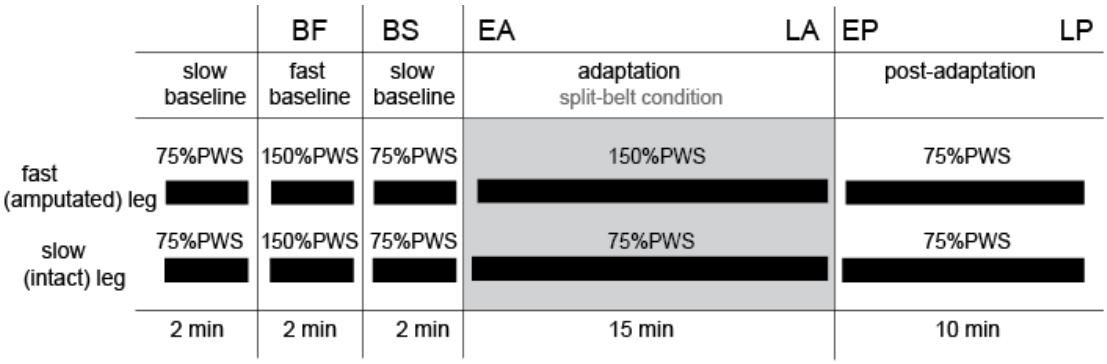

Figure 3.1: Experimental protocol (PWS - preferred walking speed; BF - fast baseline; BS – second slow baseline; EA - early adaptation; LA - late adaptation; EP - early post-adaptation; LP- late post-adaptation)

3.2.3 Data Collection and Analysis

We collected data in 2-minute increments during continuous walking trials for all experimental conditions. Gaps of 10-20 seconds between each 2-minute increment allowed for the next increment to be set up on the computer system. The first 2 minutes and last minute of adaptation and post-adaptation trials were always collected. We collected kinematic data using a six-camera motion analysis system (120Hz, VICON Motion Systems, Oxford, UK) and placed markers on the anterior and posterior superior iliac spines, greater trochanter, thigh, knee, shank, lateral malleolus, heel and second metatarsophalangeal joint of each leg. Markers were placed on the prostheses at the same locations as on the contralateral sound leg (Silverman, et al. 2008, Morgenroth, et al. 2011). We collected GRF with mechanically isolated force plates beneath each treadmill (1080Hz, AMTI, Watertown, MA, USA). Force and marker position data were low-pass filtered using a 4^{th} order Butterworth filter with a 10Hz cutoff frequency.

We calculated positive external work (W^+, Eq 1) and collisional energy loss (W_{loss}, Eq 2) of each leg on the CoM by integrating leg power, the dot product of GRF and CoM velocity (v_{com}), as has been done previously (Donelan, Adamczyk, Kuo, 2002b.

We also summed net work values of the fast leg (W_{fast}) and slow leg (W_{slow}) to find net work (ΣW; Eq 3).

$$W^{+} = \int^{+} GRF \cdot v_{com}\, dt \quad \text{Eq (1)}$$

$$W_{loss} = \int^{-} GRF \cdot v_{com} dt \quad \text{Eq (2)}$$

$$\sum W = W_{fast} + W_{slow} \quad \text{Eq (3)}$$

Where

$$W_{fast} = W^{+}_{fast\ trail\ STS} + W^{+}_{fast\ pendular} - W_{loss\ fast\ lead\ STS} \quad \text{Eq (3a)}$$

and

$$W_{slow} = W^{+}_{slow\ trail\ STS} + W^{+}_{slow\ pendular} - W_{loss\ slow\ lead\ STS} \quad \text{Eq (3b)}$$

We determined integration constants by setting average vertical CoM velocity to zero, and average anterior-posterior CoM velocity was set to belt speed. This resulted in one CoM velocity for each leg. We also calculated the sum of the individual work from both legs across a stride (Eq 3), as a measure of total work done by the subject. The subscripts refer to the leg and phase of gait for which work was calculated. Positive and negative integrals were calculated in Matlab (MathWorks, Natick, MA) using the trapz function. We calculated work during pendular phase for each leg and during the fast-leading and slow-leading STS. Bounds of integration for each phase were the times minimum and maximum vertical v_{com}, which roughly correspond to heel strike and toe off, respectively (Adamczyk and Kuo, 2009). Representative subject data for GRF and leg power can be found in the appendix (Figures A3 through A8). To prevent differences in body size from affecting the data, we normalized all work by leg length and body weight.

The calculation of work by the legs on the CoM when simultaneously walking on treadmill belts of different speeds depends upon the selection of the integration constant. As we are primarily interested in using biomechanics to explain the physiological cost of split-belt treadmill walking, we used a separate integration constant for each leg based upon the respective belt speed from the leg of interest (von Ingen Schenau, 1980). For tied-belt conditions, this approach would not cause any difference in individual leg work

calculations and measures of total work compared to previous work (Donelan, Kram, Kuo, 2001; Donelan, Kram, Kuo, 2002b). This would not be the case for the split-belt conditions, however, where the individual leg work on the CoM was calculated from a different reference frame for each leg. Using different reference frames for each leg describes what each leg is experiencing physiologically with regard to mechanical and metabolic work being done by the leg muscles. For example, the fast leg gastrocnemius activity is much higher than that of the slow leg throughout split-belt adaptation (Finley, Bastian and Gottschall, 2013), suggesting that the fast leg expends more energy. Therefore, using different reference frames accounting for the speed of each respective belt better represents the mechanical work done by the respective leg muscles.

We calculated positive work at each joint by integrating joint power, the dot product of the angular velocity ($\boldsymbol{\omega}_{joint}$) and moment ($M_{joint}$), at each joint (Eq 5).

$$W_{joint} = \int^{+} M_{joint} \cdot \omega_{joint}\, dt \qquad \text{Eq (5)}$$

We found joint moments with inverse dynamics, using included joint angles for the ankle and knee and the thigh segment angle for the hip. We calculated joint work values over different time intervals representing different important portions of the gait cycle: STS, pendular phase, and all of stance phase. Joint powers of representative subjects can be found in the appendix (Figures A9, A10).

To find absolute CoM position in a fixed (laboratory) reference frame, we averaged the anterior-posterior position of pelvic markers at each percentage of the gait cycle. We subtracted CoM position at the end of single support (contralateral heel strike) from CoM position at the beginning of single support (contralateral toe off) to find the overall anterior-posterior CoM displacement during the single support phase of gait (ΔCoM). We calculated step length symmetry (SLS, Eq 6) following the established method (Reisman et al. 2005, other refs), in which a step length (SL) is defined as the distance between heel markers at heel strike.

$$SLS = (SL_{fast\ leading} - SL_{slow\ leading})/(SL_{fast\ leading} + SL_{slow\ leading}) \qquad \text{Eq (6)}$$

We also calculated the change in kinetic energy (ΔKE) that occurred when subjects stepped from slow belt to fast belt during split-belt adaptation, switching from a fast belt reference frame to a slow belt reference frame:

$$\Delta KE = \frac{1}{2}m(v_{fast} - v_{slow})^2 \qquad \text{Eq (7a)}$$

where m is body mass in kg. For this study, the fast treadmill belt speed (v_{fast}) was 2 times the slow belt speed (v_{slow}), so equation 7a reduces to

$$\Delta KE = \frac{1}{2}m(v_{fast} - \frac{v_{fast}}{2})^2 = \frac{1}{8}m(v_{fast})^2 \qquad \text{Eq (7b)}$$

To find the average change in kinetic energy across subjects, we averaged fast belt speed and body mass across each group of subjects to get velocities and masses for equation 7a.

3.2.4 Statistical Analysis

We performed statistical analyses with SPSS (IBM, Armonk, NY, USA), defining early and late adaptation as the averages of the first 5 steps after subjects released the handrail and the last 5 steps of adaptation, respectively. Early and late post-adaptation were defined the same way, and we compared data from these times to the averages of the last 5 steps of each baseline trial. For step length symmetry and CoM position, we used repeated measures ANOVA (rmANOVA) followed by pairwise comparisons with Bonferroni corrections to compare all trials. Three rmANOVAs were performed for each work variable: one rmANOVA compared the fast leg in trials when it moved at 150% PWS (base fast, early adaptation, late adaptation), another compared the fast leg when it moved at 75%PWS (base slow, early post-adaptation, late post-adaptation), and the third compared slow leg work in all trials but base fast. After analyzing CoM position, we performed post-hoc, paired t-tests to compare the sum of leg work between early and late adaptation. All statistical tests were performed with an alpha level of 0.05.

3.3 Results

All subjects displayed stereotypical responses in step kinematics compared to previous work. Compared to slow baseline, both controls and amputees exhibited

negative step length asymmetry (longer steps with slow leg leading) in early adaptation (controls: p=0.034; amputees: p=0.013) and positive asymmetry in early post-adaptation (controls: p=0.031; amputees: p=0.031). Both groups returned to baseline step length symmetry in late adaptation and late post-adaptation (Figure 3.2). The difference between step length symmetry in early and late post-adaptation approached significance for amputees (p=0.097).

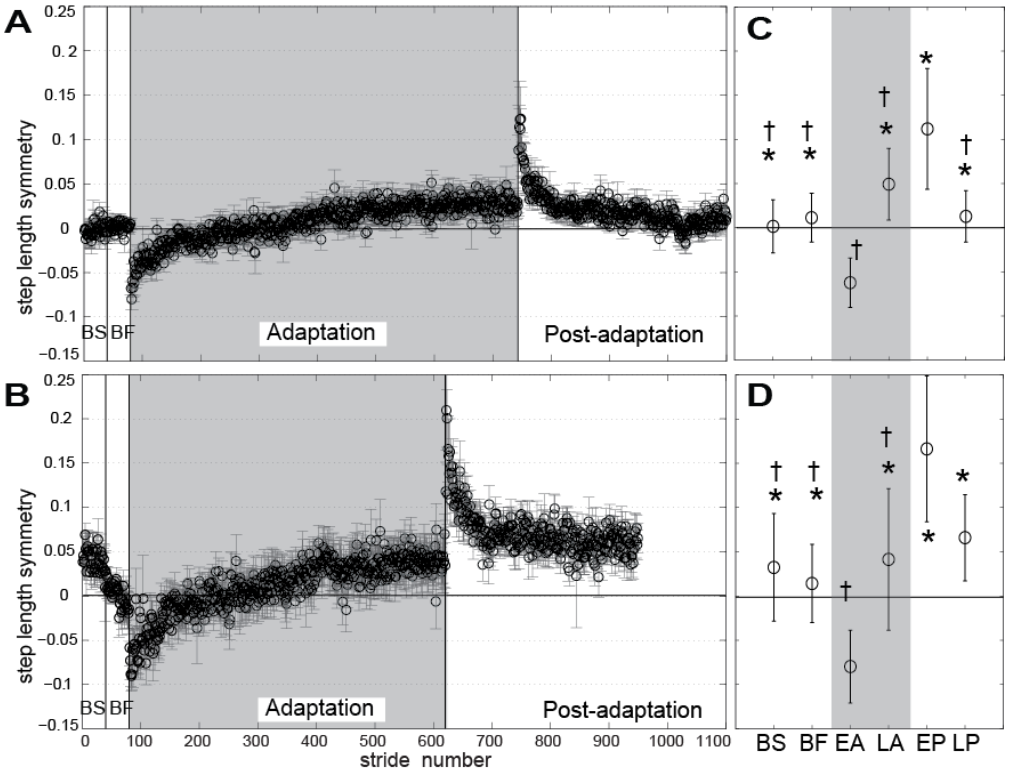

Figure 3.2: Step length symmetry for able-bodied control subjects (A & C) and trans-tibial amputees (B & D). C and D display averages of the last 5 steps of each baseline trial (BS, BF) and the first and last 5 steps of adaptation (EA, LA) and post-adaptation (EP, LP). * indicates significant difference ($p<0.05$) from early adaptation and † indicates significant difference ($p<0.05$) from early post-adaptation. Vertical bars indicate standard error across subjects.

The initial response of all subjects during early adaptation to split-belt treadmill walking is characterized by an increase in propulsive work, primarily by the hip joint, during single limb stance. Controls displayed a pattern in fast ankle work during stance, which was significantly higher than fast baseline in early adaptation (p=0.010) and lower

than slow baseline in early post-adaptation (p=0.010), but returned to baseline levels in late adaptation and late post-adaptation (Figure 3.3A, C). Both hip work (p=0.036) and ankle work (p=0.015) of the controls' fast leg decreased significantly between early and late adaptation. Controls also altered fast ankle work timing between early and late adaptation, decreasing the ankle work done in pendular phase and increasing the percentage of ankle work done by the trailing leg in STS (p=0.006;Figure 3.4A, C). In contrast, amputees showed no significant changes in fast (prosthetic) ankle work (Figure 3.3B, D) or ankle work timing (Figure 3.4B, D). While amputees did not alter hip work over the course of adaptation, they used significantly less hip work in stance during adaptation than in the fast baseline trial.

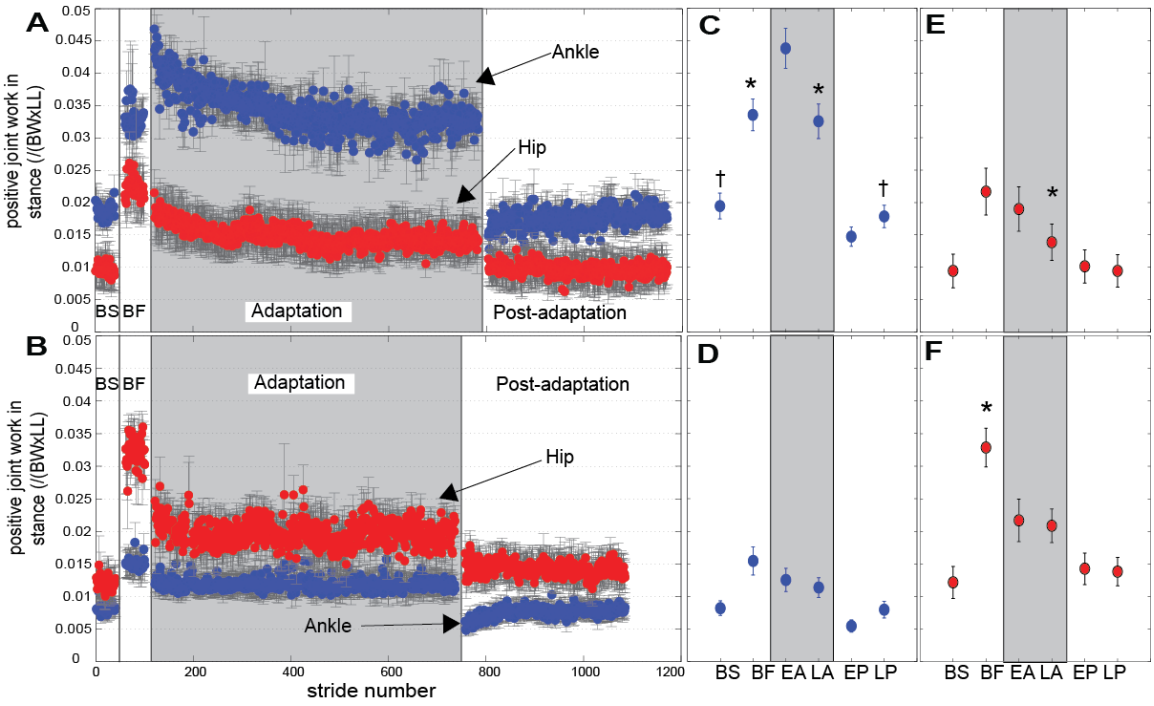

Figure 3.3: Fast leg ankle work (blue circles) and hip work (red circles) during stance for controls (A, C and E) and trans-tibial amputees (B, D and F). C and D display averages of ankle work in the last 5 steps of each baseline trial (BS, BF) and the first and last 5 steps of adaptation (EA, LA) and post-adaptation (EP, LP). E and F display hip work averaged over the same strides * indicates significant difference (p<0.05) from early adaptation. Vertical bars indicate standard error across subjects.

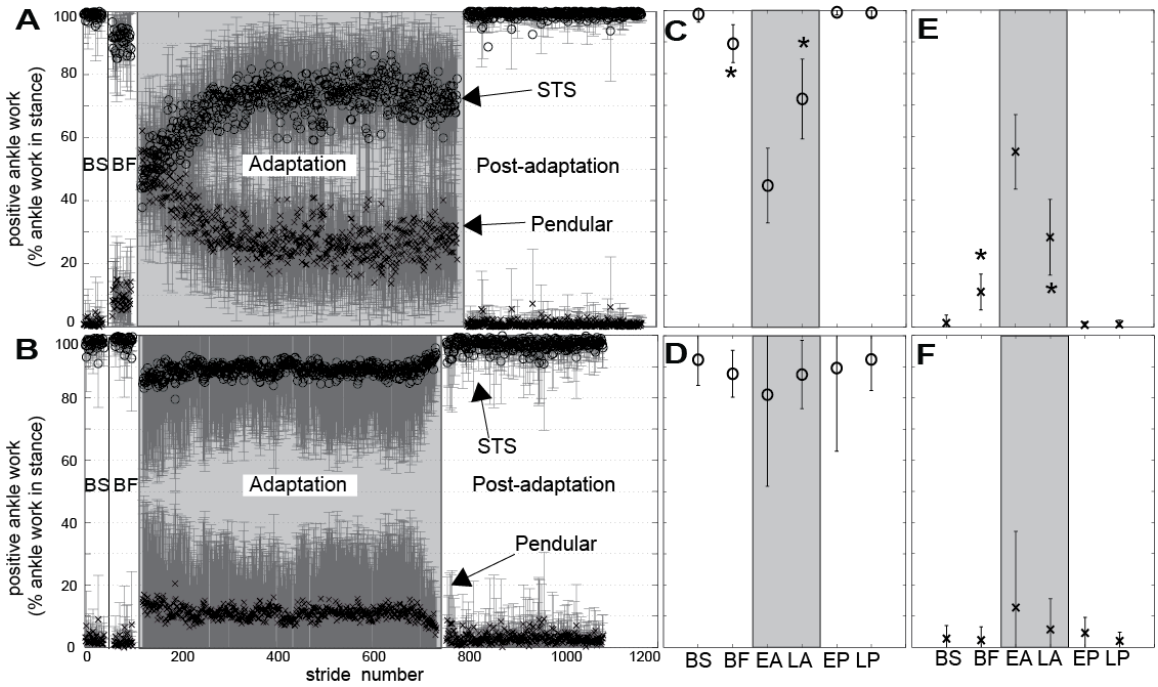

Figure 3.4: Percentage of fast ankle work done during pendular phase (x) or step-to-step transition (o) for controls (A, C and E) and trans-tibial amputees (B, D and F). C and D display averages of trailing ankle work in STS over the last 5 steps of each baseline trial (BS, BF) and the first and last 5 steps of adaptation (EA, LA) and post-adaptation (EP, LP). E and F display ankle work during pendular phase averaged over the same strides. * indicates significant difference ($p<0.05$) from early adaptation. Vertical bars indicate standard error across subjects.

All subjects decreased positive work during pendular phase and increased collisional energy loss of the fast leg as they adapted to split-belt walking. Controls and amputees altered collisional energy loss of the fast leading leg in STS over the course of both adaptation and post-adaptation (Figure 3.5). In early adaptation, controls had a lower magnitude of collisional energy loss than in fast baseline ($p<0.001$), but this significantly increased back to baseline levels by late adaptation ($p=0.001$; Figure 3.5A, C). In early post-adaptation, controls had a higher collisional energy loss than in slow baseline ($p=0.001$), which significantly decreased to baseline in late post-adaptation ($p=0.014$). Amputees showed the same pattern of changes in collisional energy loss across trials as controls (Figure 3.5B, D), with the exception that the difference in energy loss between slow baseline and early post-adaptation only approached significance ($p=0.054$). For controls, positive work of the fast leg during pendular phase was significantly higher in

early adaptation than either fast baseline or late adaptation (p=0.004; Supplemental Figure A3.1A, C), whereas amputees performed less fast (prosthetic) leg pendular work in late adaptation than fast baseline (Figure A3.1B, D). Neither group of subjects showed significant changes over adaptation in positive work of the fast trailing leg during STS (Fig S2), although controls performed significantly less positive, fast trail work in early post-adaptation than in the slow baseline or late post-adaptation (Figure A3.2C). Net positive work across both legs showed no significant changes between early and late adaptation. Slow leg work data are reported in the supplement (Tables A3.1-4). Notably, both amputees and controls had significantly higher positive pendular phase work by the slow leg throughout adaptation than in the slow baseline trial (Table A3.2).

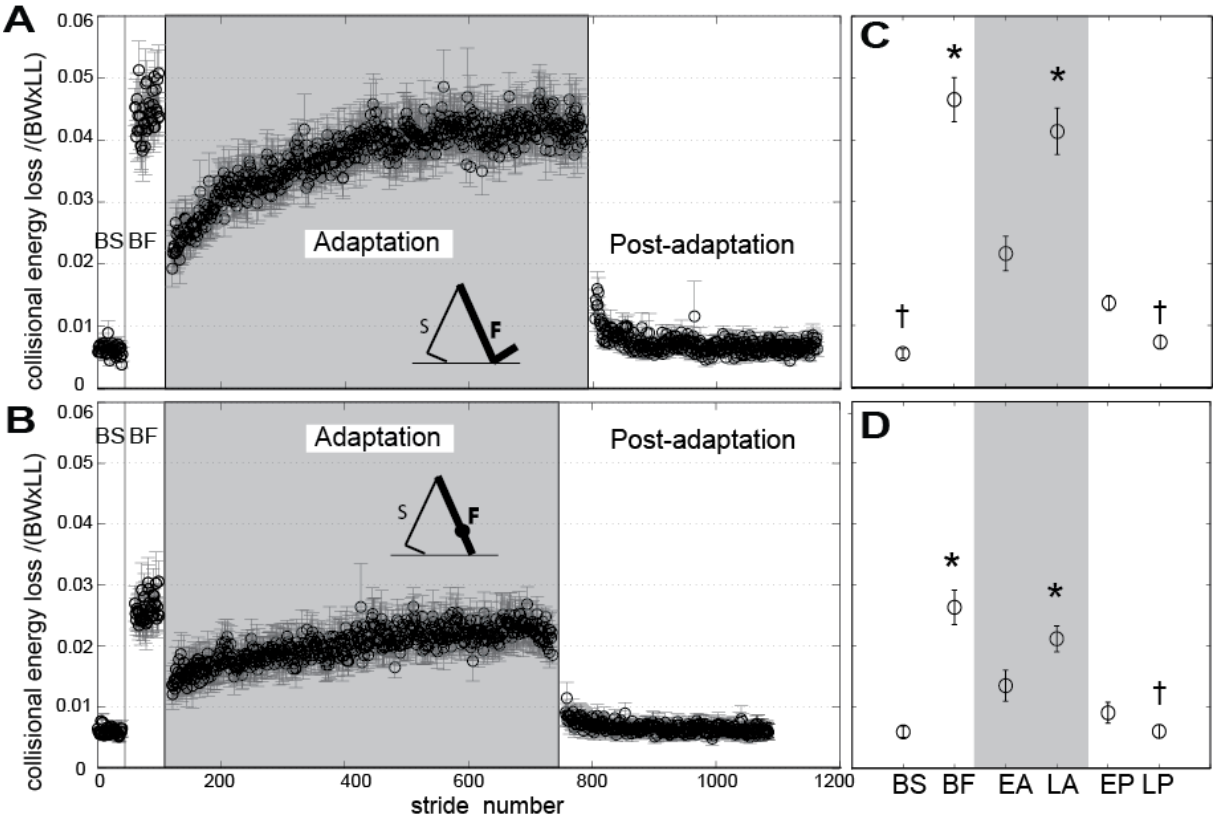

Figure 3.5: Collisional energy loss at the fast leading leg during STS for able-bodied control subjects (A and C) and trans-tibial amputees (B and D). C and D display averages of the last 5 steps of each baseline trial (BS, BF) and the first and last 5 steps of adaptation (EA, LA) and post-adaptation (EP, LP). * indicates significant difference ($p<0.05$) from early adaptation and † indicates significant difference ($p<0.05$) from early post-adaptation. Vertical bars indicate standard error across subjects.

As they adapted to split-belt walking, all subjects adopted asymmetric CoM movement patterns in the fixed (laboratory) reference frame. Compared to early adaptation, both controls and amputees began to move farther backwards on the treadmill during the single support phase by late adaptation (Figure 3.6). Subjects compensated for backward CoM displacement during single support with forward movements during slow leg single support to maintain overall CoM position in the fixed (laboratory) reference frame during baseline, adaptation and post-adaptation (Figure 3.7). Interestingly, by late adaptation the backward CoM displacement during single support in all subjects became asymmetric, with greater posterior displacement on the fast belt (controls: $p=0.033$; amputees: $p=0.013$) and less displacement on the slow belt compared to baseline (controls: $p=0.007$; amputees: $p=0.021$). This change happened more quickly in amputees and more slowly in controls. Transitioning from the fast belt to the slow belt reduced kinetic energy by an average of 37.7J for control subjects and 30.6J for amputees. Notably, subjects moved backwards in both single support periods in baseline trials. They moved forward during double support periods, but the amount of forward displacement was unchanged in adaptation (data not shown). We also found that between early and late adaptation, the sum of the individual work from both legs decreased significantly for controls ($p=0.0011$), and amputees ($p=0.0453$).

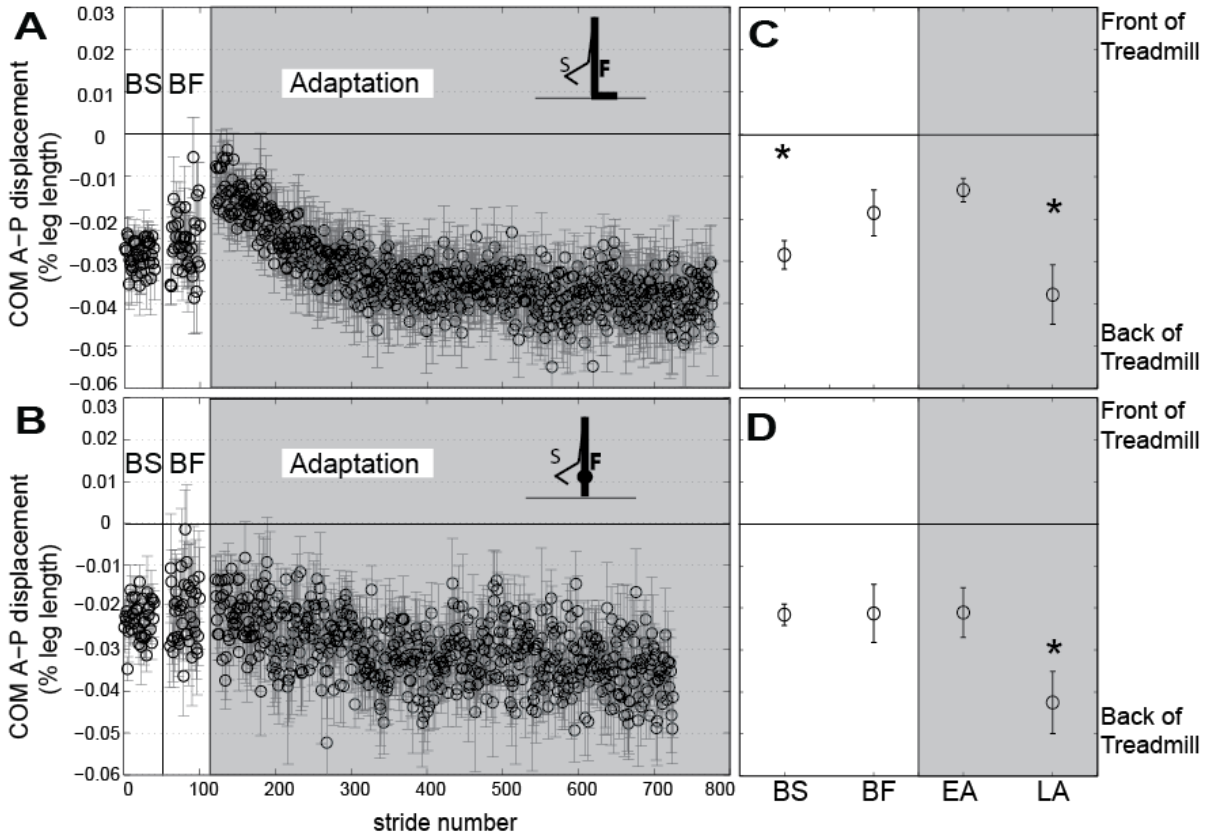

Figure 3.6: Center of mass (CoM) displacement in a fixed reference frame during fast leg single support for controls (panels A and C) and trans-tibial amputees (x, panels B and D). C and D display averages of the last 5 steps of each baseline trial (BS, BF) and the first and last 5 steps of adaptation (EA, LA). * indicates significant difference ($p<0.05$) from early adaptation. Vertical bars indicate standard error across subjects.

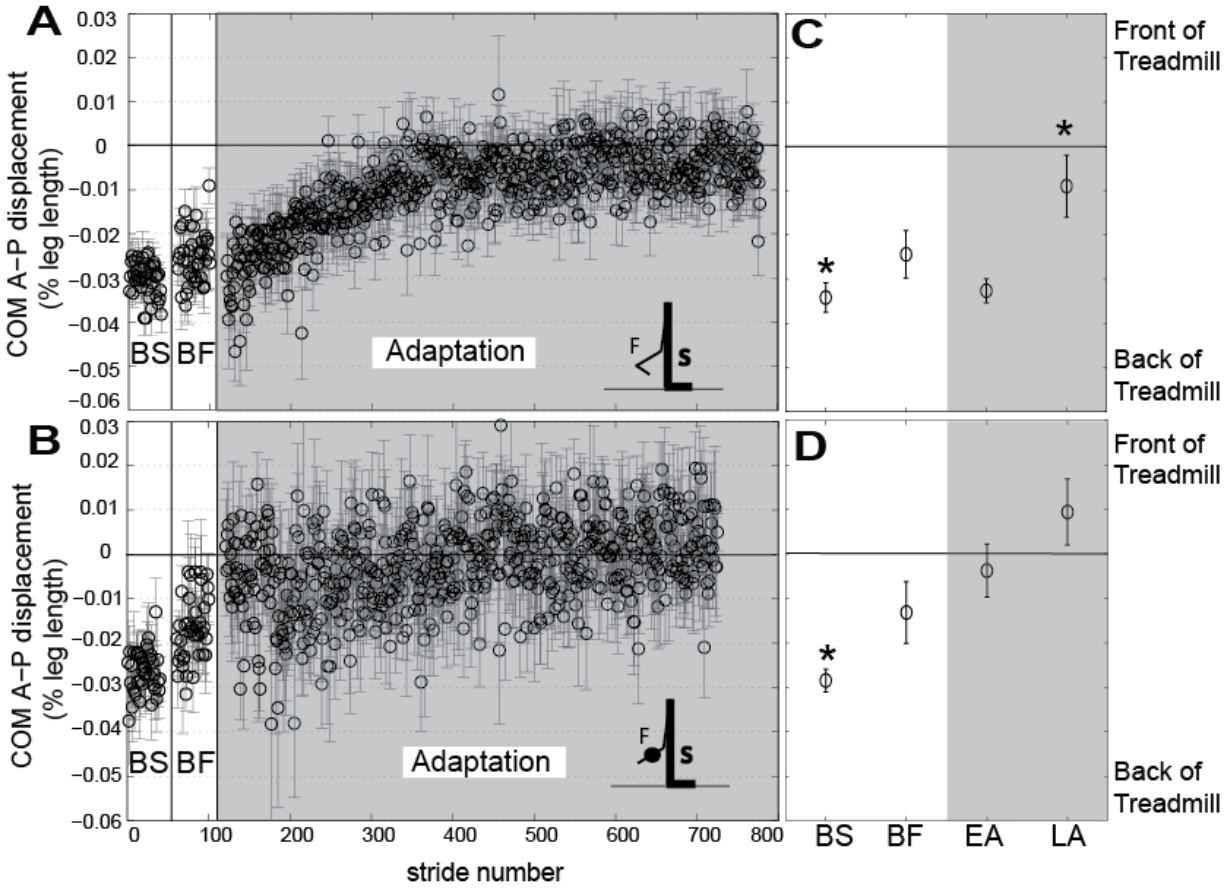

Figure 3.7: Center of mass (CoM) displacement in a fixed reference frame during slow leg single support for controls (panels A and C) and amputees (panels B and D). C and D display averages of the last 5 steps of each baseline trial (BS, BF) and the first and last 5 steps of adaptation (EA, LA). * indicates significant difference ($p<0.05$) from early adaptation. Vertical bars indicate standard error across subjects.

3.4 Discussion

3.4.1 Step length symmetry has typical adaptation pattern in both controls and amputees

For all subjects, step length symmetry changed in a way that was consistent with healthy subjects' behavior in previous studies (Reisman, Block, Bastian, 2005; Malone, Bastian, 2014; Vazquez et al. 2015; Huynh et al. 2014). Both controls and amputees initially responded to split-belt walking by taking longer steps with the slow leg leading (negative step length asymmetry, but returned to baseline step length symmetry levels by late adaptation. In early post-adaptation, both groups had an aftereffect positive step length asymmetry, but they returned again to their baseline asymmetry in late post-

adaptation. This aftereffect and the gradual changes in adaptation and post-adaptation are indicative of feedforward control. Because this adaptation was driven by feedforward control, the lack of sensory feedback in the amputees' distal limb did not impede the ability to adapt step length symmetry.

3.4.2 Controls switch to trailing ankle work for propulsion during split-belt adaptation

The data support the hypothesis that, for control subjects, the fast leg hip work would decrease and trailing ankle work during STS would increase during split-belt walking adaptation. As fast hip work decreased, ankle work switched from being performed mostly during pendular phase of gait to being performed primarily in late stance. Furthermore, controls decrease fast leg work on the CoM in pendular phase as they adapt. The changes in hip work, ankle work and pendular phase work all occur gradually over the course of adaptation, suggesting that they are driven by feedforward control rather than an immediate response to sensory feedback. Experimental and modeling studies demonstrate that trailing leg ankle work during STS is up to four times more efficient than hip work during pendular phase (Kuo, 2002; Yeom, Park, 2011, Donelan 2002a, Donelan, 2002b, Oh et al, 2012), so switching from hip work and ankle work in pendular phase to primarily providing propulsion with the trailing ankle work is likely a contributor to the increased mechanical efficiency (Thajchayapong et al. in prep) and reduced metabolic (Finley, Bastian, Gottschall, 2013) power observed during adaptation to split-belt walking.

Amputees had no changes in fast (prosthetic) ankle and fast hip work over the course of adaptation. Although amputees had no active control over their prosthetic ankles, they increased collisional energy loss at heel strike, which could have loaded the spring in the prosthesis. However, the lack of change in positive ankle work suggests that whatever energy was stored in the prosthesis at heel strike did not significantly increase ankle work at toe off. Similarly, amputees were unable to modulate the timing of their prosthetic ankle work.

Unlike fast ankle work, increases in fast trailing leg work on the CoM were not significant across adaptation for controls, which did not support the hypothesis. Although these increases were not significant, our previous work showed that healthy subjects

significantly increased fast trailing leg work during split-belt walking adaptation with a 3:1 belt speed ratio (Thajchayapong et al. in prep). Since smaller belt speed ratios result in less dramatic adaptive changes in kinematics (Reisman, Block, Bastian, 2005), it is likely that using a 2:1 belt speed ratio caused smaller changes in positive work as well. Additionally, we excluded data from the first 30 seconds of adaptation and post-adaptation, because a few subjects pushed or pulled on the handrail they were holding, which skewed GRF and work data. Holding the handrail was necessary for the safety of our amputee subjects and to be consistent in our treatment of our control subjects. Adaptive changes in locomotion, however, occur most rapidly within the first minute of adaptation and in post-adaptation. This is likely the reason why we found few statistically significant changes between early and late post-adaptation, when changes probably occurred more quickly than in adaptation (Malone, Bastian, 2010, Bastian 2008, Selgrade, Chang 2015). Given that we excluded the first 30 seconds of adaptation and post-adaptation, subjects must have adapted ankle work timing and pendular phase work in robust, gradual changes for us to detect a significant difference between early and late adaptation, or between early and late post-adaptation.

3.4.3 Collisional energy loss and center of mass displacement

In both amputees and controls, collisional energy loss exhibited a typical pattern of adaptation. Collisional energy loss during fast leading STS decreased in early adaptation, and then increased back to baseline by late adaptation. Collisional energy loss in early post-adaptation showed an aftereffect, increasing above slow baseline levels for controls, and both groups decreased collisional energy loss between earl and late post-adaptation. These gradual changes in adaptation and post-adaptation suggest that collisional energy loss is under feedforward control. Feedforward adaptation of collisional energy loss is consistent with feedforward adaptation of posterior braking GRF and vertical GRF (Mawase et al. 2013; Ogawa et al. 2014), which are used to calculate collisional energy loss. Our results are also consistent with increased braking force at increased speed (Park, Park, 2013), since negative work in late split-belt adaptation is no different than the fast tied-belt baseline collisional energy loss. However, during normal walking, propulsive force also usually increases with speed (Park, Park, 2013), and we expect collisional energy losses to be minimized so that subjects do not

have to expend energy to make up for lost energy in braking (Ruina, Bertram, Srinivasan, 2005). Given these findings in tied belt treadmill and overground walking, how can subjects walking on a split-belt treadmill simultaneously increase collisional energy loss while decreasing metabolic power as they adapt?

After further data analysis, we discovered a second locomotor adaptation strategy related to anterior-posterior COM position control that is unique to split-belt treadmill walking and may explain some of the observed changes in mechanical and metabolic power. This is the first observation that subjects use a COM displacement strategy that exploits a characteristic unique to split-belt treadmill walking to decrease energetic costs. Subjects allow their CoM to move further backwards in a fixed (laboratory) reference frame when only on the fast belt, remain stationary when only on the slow belt, and regain forward COM position during STS. In a fixed reference frame during baseline trials, subjects typically move backwards during both single support phases and move forward during STS to maintain their position on the treadmill. By late split-belt adaptation, however, all of our subjects primarily moved further backwards during single support on the fast belt, meaning they were effectively walking slower than the fast belt speed. They kept their CoM largely stationary during single support on the slow belt. The benefit of using this asymmetric CoM displacement strategy is that it is energetically less expensive to propel oneself forward (relative to the belt) at lower velocity than to propel oneself forward at higher velocity. This point is supported by a change in kinetic energy of over 30J when subjects switch from one belt to the other. The change in energy simply caused by switching belts is substantial. For comparison, consider that, for walking at 1.25m/s, overall positive CoM work per step is only approximately 21.7± 2.2J (Kuo, Donelan, Ruina, 2005).

The high CoM displacement in slow single support can also explain why subjects would have such high collisional energy loss during split-belt adaptation. The CoM is essentially stationary in a fixed reference frame during slow leg single support and then abruptly contacts a fast moving belt, and a large collisional energy loss is required to move backward with the fast belt. Based on CoM displacement, it appears that both groups of subjects waited until they were on the slow belt to make up for the large collisional energy loss on the fast belt. Allowing more backward CoM displacement on

the fast belt is another possible contributor to the reduction in metabolic power previously observed during split-belt walking adaptation (Finley, Bastian, Gottschall, 2013).

We had hypothesized that, as amputees adapted to split-belt walking, they would rely more on the slow (intact) leg, but all subjects had higher slow pendular leg work throughout adaptation than in the slow baseline. Both groups also used the CoM displacement strategy of increasing backward movement on the fast belt and decreasing backward movement on the slow belt. The difference was that amputees adapted to this strategy more quickly compared to control subjects. Having the prosthesis on the fast belt made large increases in fast trailing ankle work impossible for amputees, so they quickly began relying on their intact leg on the slow belt in order to stay on the treadmill. Amputees generally rely on their intact leg as a gait compensation strategy (Houdijk et al. 2009; Adamczyk, Kuo 2015; Silverman et al. 2008), so this may have made transitioning to the slow (intact leg) when adapting to split-belt walking more automatic for amputees than controls.

3.5 Conclusions

In conclusion, control subjects adapt to split-belt walking by exploiting two strategies that may contribute to improved efficiency and reduced metabolic cost: they increase the percentage of fast ankle work during STS while reducing inefficient hip work and they allow their CoM to move backward during single support on the fast belt, while limiting backward motion on the slow belt. Because trans-tibial amputees in this study did not have a powered ankle on the fast belt, they had to quickly rely on the alternative COM displacement strategy slow throughout adaptation.

A3 Appendix: ADDITIONAL DATA FOR CHAPTER 3

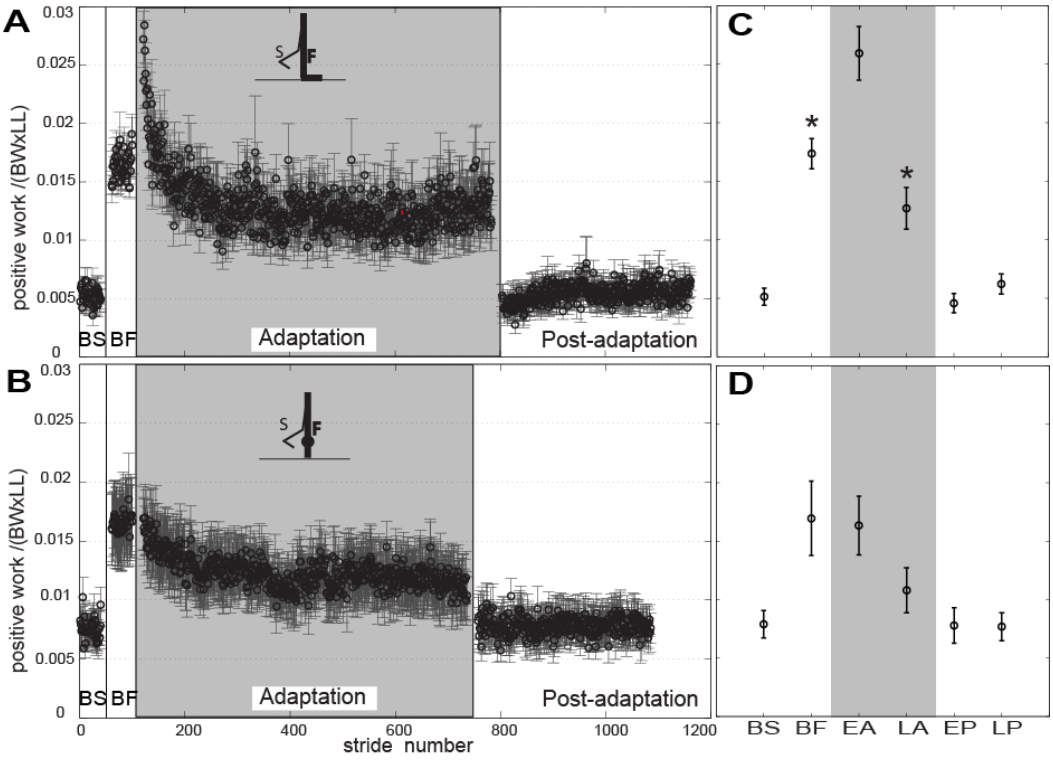

Fig A3.1: Positive work of the fast (prosthetic) leg during pendular phase for able-bodied control subjects (A and C) and trans-tibial amputees (B and D). C and D display averages of the last 5 steps of each baseline trial (BS, BF) and the first and last 5 steps of adaptation (EA, LA) and post-adaptation (EP, LP). * indicates significant difference ($p<0.05$) from early adaptation. Vertical bars indicate standard error across subjects. The difference between EP and LP for controls approached significance ($p=0.051$), as did the difference in EA and LA for amputees ($p=0.057$).

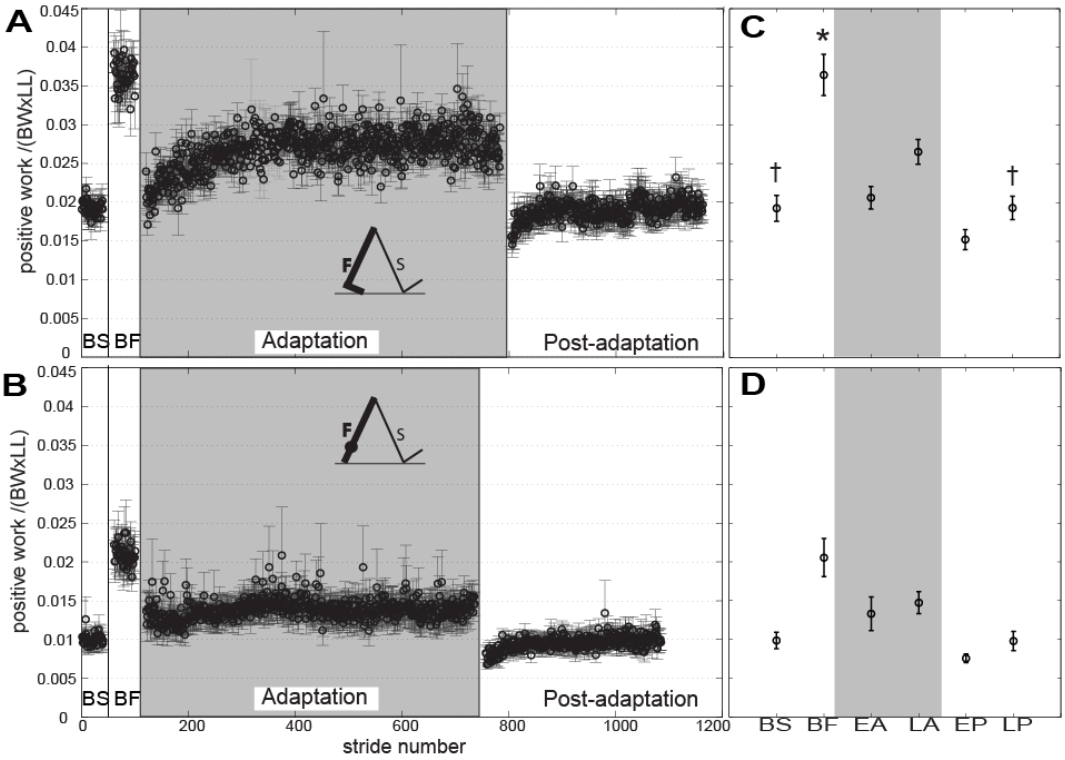

Fig A3.2: Positive work of the fast (prosthetic) trailing leg during the step-to-step transition for able-bodied control subjects (A and C) and trans-tibial amputees (B and D). C and D display averages of the last 5 steps of each baseline trial (BS, BF) and the first and last 5 steps of adaptation (EA, LA) and post-adaptation (EP, LP). * indicates significant difference ($p<0.05$) from early adaptation and † indicates significant difference ($p<0.05$) from early post-adaptation. Vertical bars indicate standard error across subjects.

Supplementary Tables:

All significant differences in "slow" leg work on the center of mass and all significant differences in work performed by joints of the slow leg are displayed in the tables below. Each cell is labeled NS (non-significant, $p>0.10$) or with "mean difference (p-value)". Differences that approach significance *($0.05<p<0.10$)* are italicized. Mean differences were calculated as row – column (e.g. BS – EA appears in the first cell of Table S1).

Table A3.1: Hip work of slow leg in stance (normalized by body weight & leg length)

Controls	**BS**	**EA**	**LA**	**EP**	**LP**	
BS	_	-0.007 (0.001, p=0.008)	-0.006 (0.002, p=0.09)	-0.005 (0.001, p<0.001)	-0.006 (0.001, p=0.001)	**BS**
Amputees	**BS**	**EA**	**LA**	**EP**	**LP**	
BS	_	-0.008(0.002, p=0.013)	*-0.006 (0.002, p=0.063)*	NS	NS	**BS**
EA	_	_	NS	NS	0.010 (0.002 p=0.012)	**EA**

main effect: ctrls, p=0.001, amps p<0.001

Table A3.2: Positive work of slow leg during pendular phase (normalized by body weight and leg length)

Controls	**BS**	**EA**	**LA**	**EP**	**LP**	
BS	_	-0.009 (0.002, p=0.025)	-0.011 (0.002, p=0.002)	-0.005 (0.001, p=0.014)	NS	**BS**
EA	_	_	NS	NS	0.006 (0.002, p=0.051)	**EA**
LA	_	_	_	0.006 (0.001, p=0.028)	0.009 (0.001, p=0.001	**LA**
EP	_	_	_	_	0.003 (0.001, p=0.054)	**EP**
LP	_	_	_	_	_	**LP**
Amputees	**BS**	**EA**	**LA**	**EP**	**LP**	
BS	_	-0.013 (0.001, p<0.001)	-0.012 (0.001, p<0.001)	NS	NS	**BS**
EA	_	_	NS	0.01 (0.002, p=0.003	0.012 (0.001, p=0.001)	**EA**
LA	_	_	_	0.010 (0.001, p=0.002)	0.012 (0.001, p<0.001	**LA**
EP	_	_	_	_	NS	**EP**
LP	_	_	_	_	_	**LP**

main effect p <0.001 (ctrl), p<0.001 (amp)

Table A3.3: Positive work of slow trailing leg during STS (normalized by body weight and leg length)

Controls	**BS**	**EA**	**LA**	**EP**	**LP**	
BS	_	NS	NS	NS	NS	**BS**
EA	_	_	NS	NS	NS	**EA**
LA	_	_	_	NS	NS	**LA**
EP	_	_	_	_	-0.005 (0.001, p=0.001)	**EP**
LP	_	_	_	_	_	**LP**
Amputees	**BS**	**EA**	**LA**	**EP**	**LP**	
BS	_	*0.005 (0.001, p=0.098)*	NS	NS	NS	**BS**
EA	_	_	NS	*-0.003 (0.001 p=0.068)*	NS	**EA**
LA	_	_	_	NS	-0.005 (0.001, p=0.03)	**LA**
EP	_	_	_	_	-0.004 (0.001, p=0.037)	**EP**
LP	_	_	_	_	_	**LP**

main effect p =0.017 (ctrl), p<0.001 (amp)

Table A3.4: Collisional energy loss of slow leading leg in STS (normalized by body weight and leg length)

Controls	**BS**	**EA**	**LA**	**EP**	**LP**	
BS	_	0.018 (0.003, p=0.007)	0.012 (0.003, p=0.027)	NS	NS	**BS**
EA	_	_	NS	-0.022(0.003, p=0.003)	-0.018 (0.003, p=0.009)	**EA**
LA	_	_	_	-0.015 (0.003, p=0.019)	-0.012 (0.003, p=0.028)	**LA**
EP	–	–	–	–	NS	**EP**
LP	–	–	–	–	–	**LP**
Amputees	**BS**	**EA**	**LA**	**EP**	**LP**	
BS	_	0.023(0.004, p=0.013)	0.013 (0.002, p=0.002)	NS	NS	**BS**
EA	_	_	NS	-0.027 (0.005 p=0.017)	-0.023 (0.004 p=0.014)	**EA**
LA	_	_	_	-0.017 (0.003, p=0.006)	-0.013 (0.002, p=0.003)	**LA**
EP	–	–	–	–	NS	**EP**
LP	–	–	–	–	–	**LP**

main effect p <0.001 (ctrl), p=0.002 (amp)

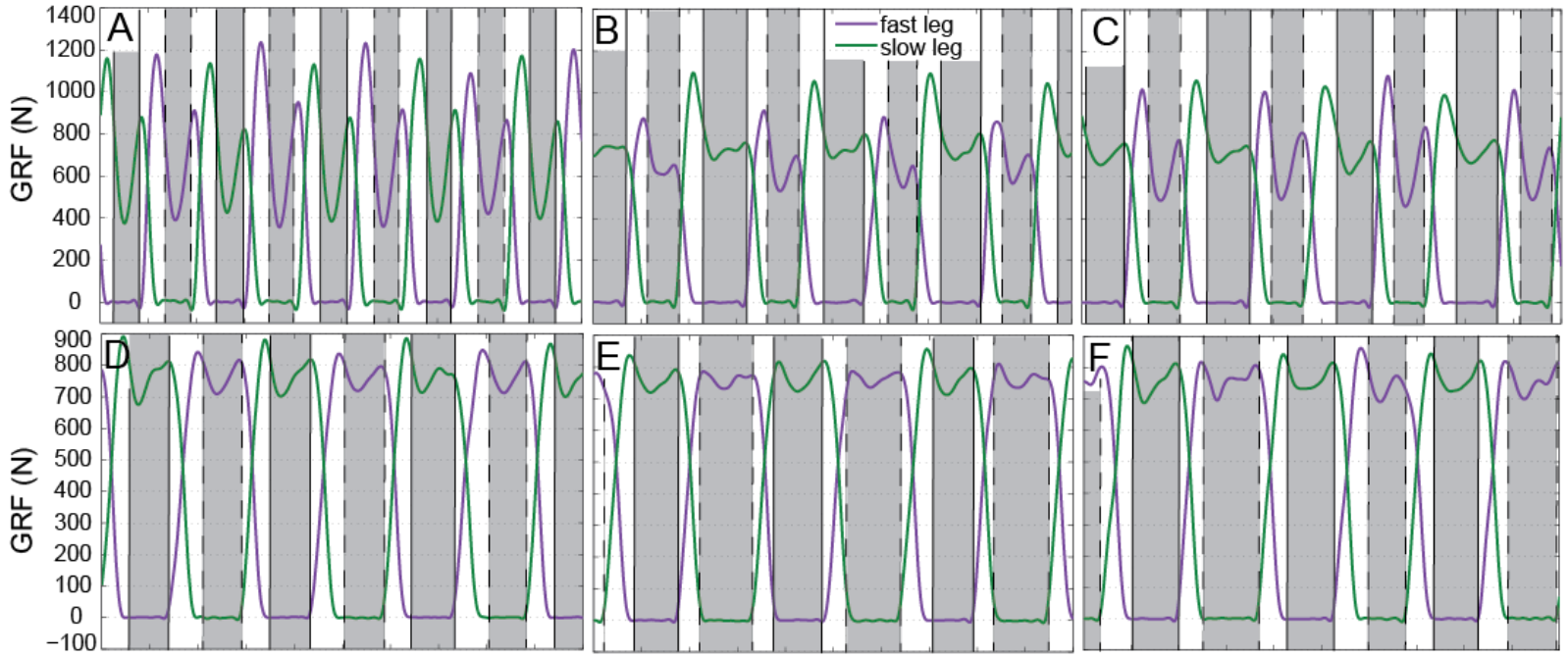

Figure A3.3: Vertical GRF from several strides for a representative control subject during fast baseline (A), early adaptation (B), late adaptation (C), slow baseline (D), early post-adaptation (E), and late post-adaptation (F). Slow leg GRF is green and fast leg GRF is in purple. Pendular phases are shaded gray, with fast leg pendular phase bounded by dashed lines and slow leg pendular phase bounded by solid lines.

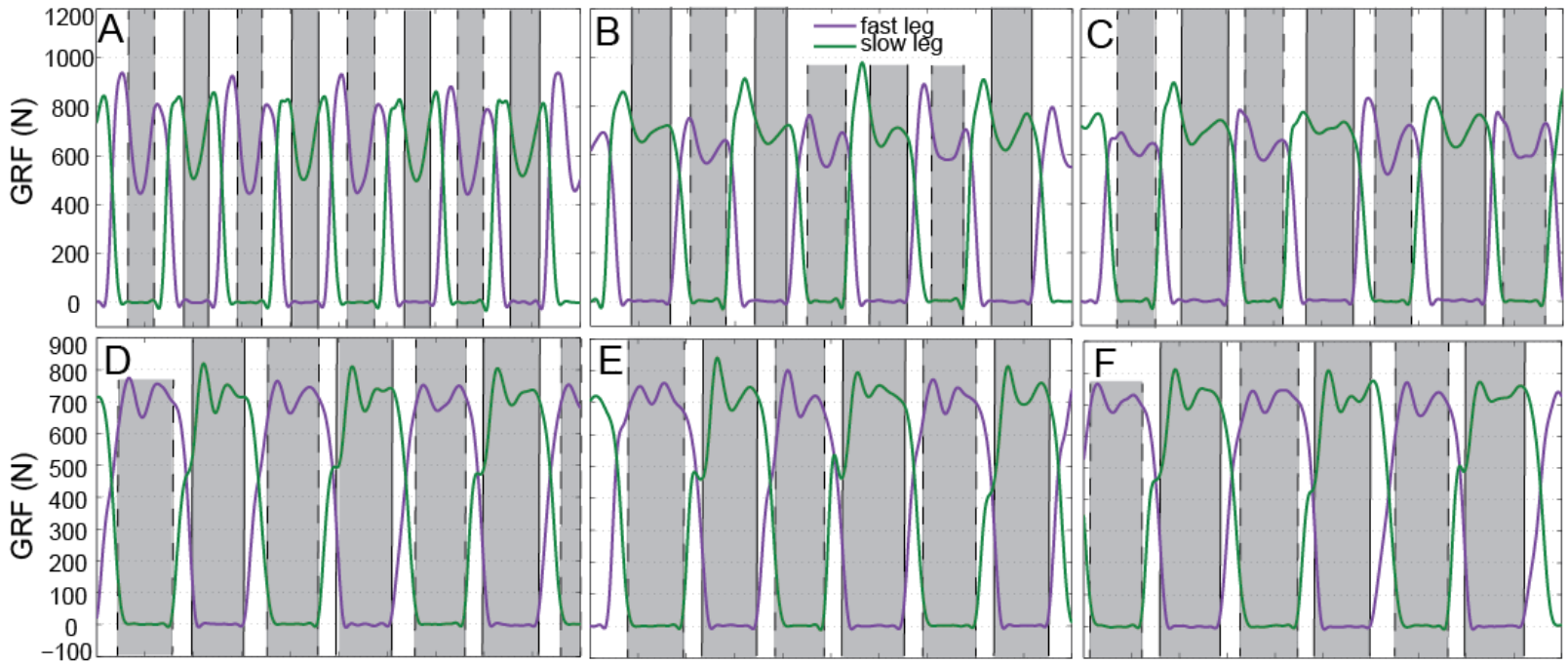

Figure A3.4: Vertical GRF from several strides for a representative amputee during fast baseline (A), early adaptation (B), late adaptation (C), slow baseline (D), early post-adaptation (E), and late post-adaptation (F). Slow leg GRF is green and fast leg GRF is in purple. Pendular phases are shaded gray, with fast leg pendular phase bounded by dashed lines and slow leg pendular phase bounded by solid lines.

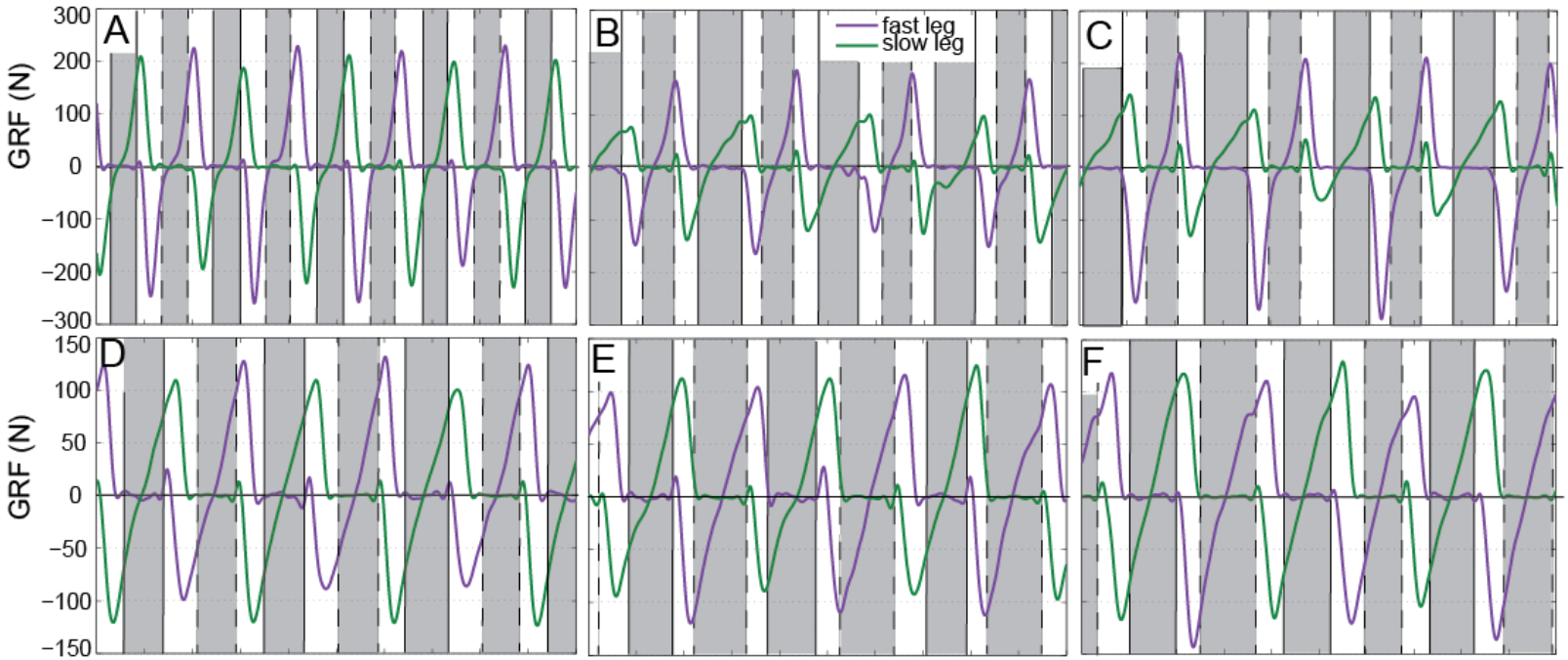

Figure A3.5: Anterior-posterior GRF from several strides for a representative control subject during fast baseline (A), early adaptation (B), late adaptation (C), slow baseline (D), early post-adaptation (E), and late post-adaptation (F). Slow leg GRF is green and fast leg GRF is in purple. Pendular phases are shaded gray, with fast leg pendular phase bounded by dashed lines and slow leg pendular phase bounded by solid lines.

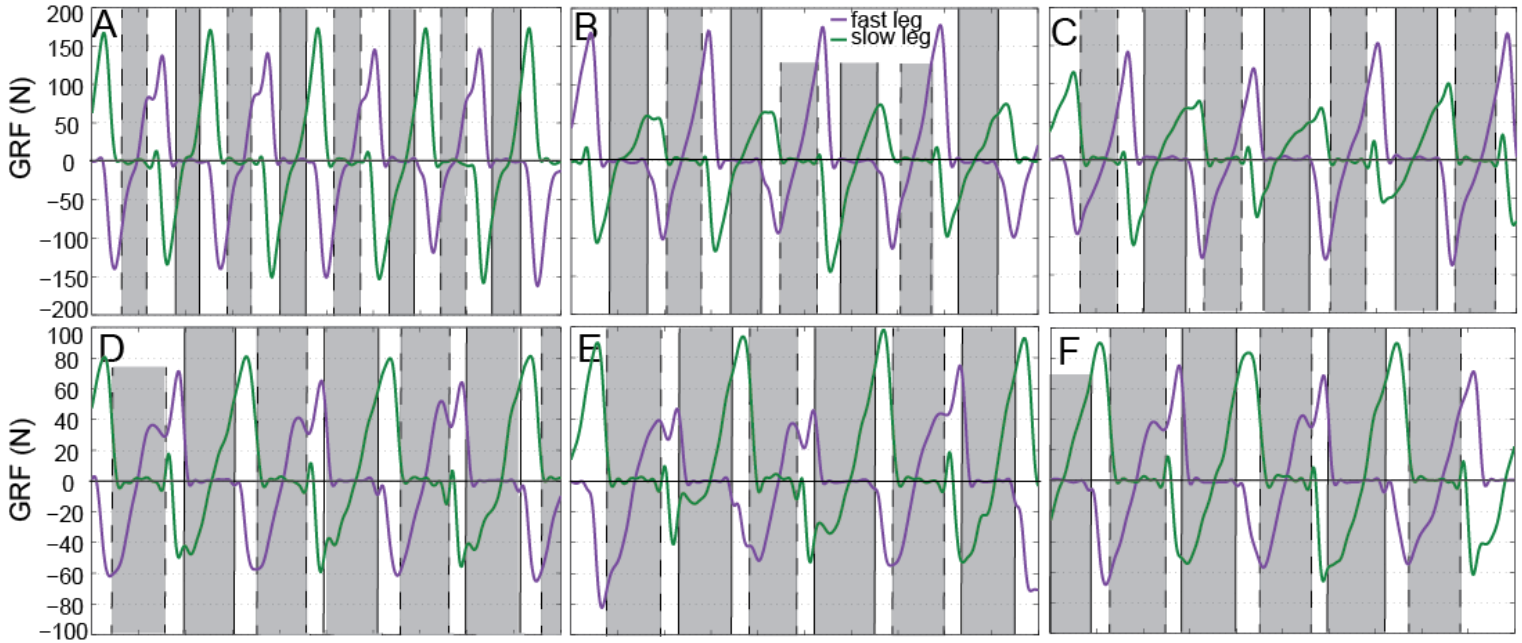

Figure A3.6: Anterior-posterior GRF for a representative amputee during fast baseline (A), early adaptation (B), late adaptation (C), slow baseline (D), early post-adaptation (E), and late post-adaptation (F). Slow leg GRF is green and fast leg GRF is in purple. Pendular phases are shaded gray, with fast leg pendular phase bounded by dashed lines and slow leg pendular phase bounded by solid lines.

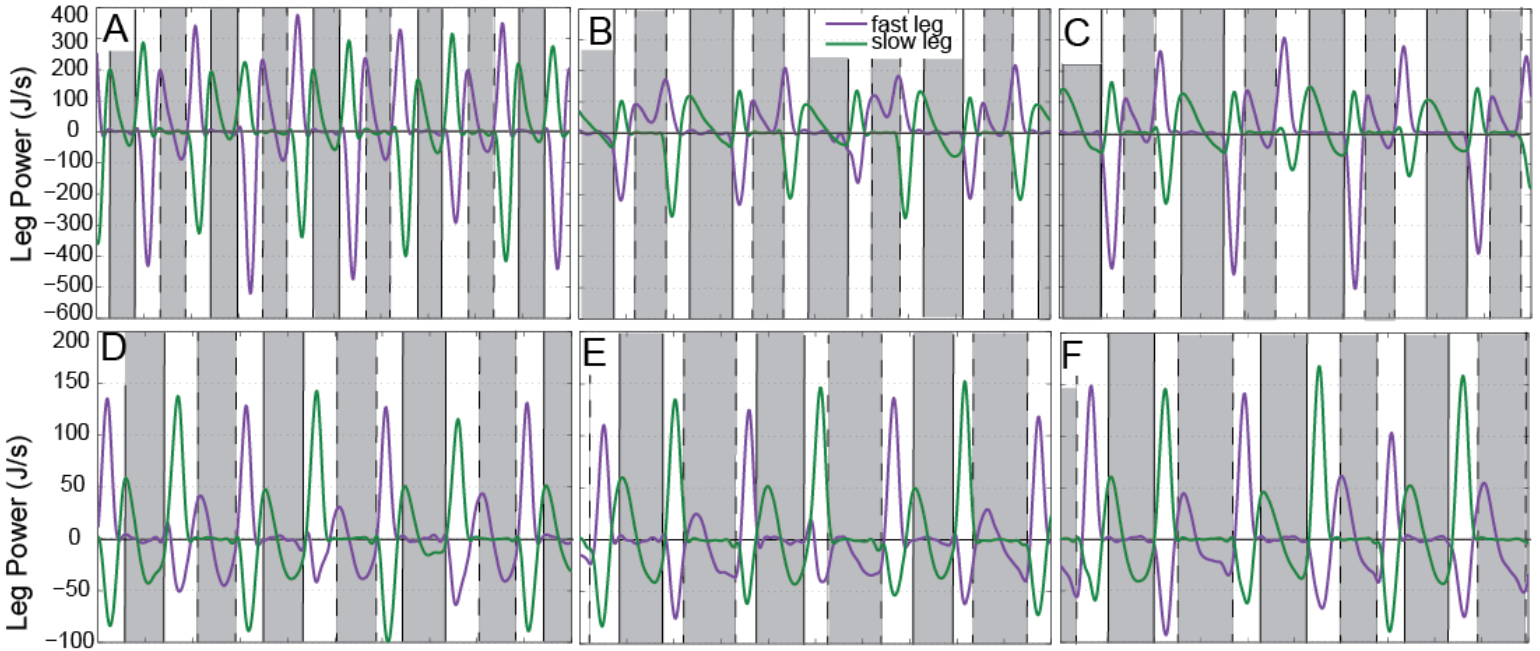

Figure A3.7: Leg power from several strides for a representative control subject during fast baseline (A), early adaptation (B), late adaptation (C), slow baseline (D), early post-adaptation (E), and late post-adaptation (F). Slow leg power is green and fast leg power is purple. Pendular phases are shaded gray, with fast leg pendular phase bounded by dashed lines and slow leg pendular phase bounded by solid lines.

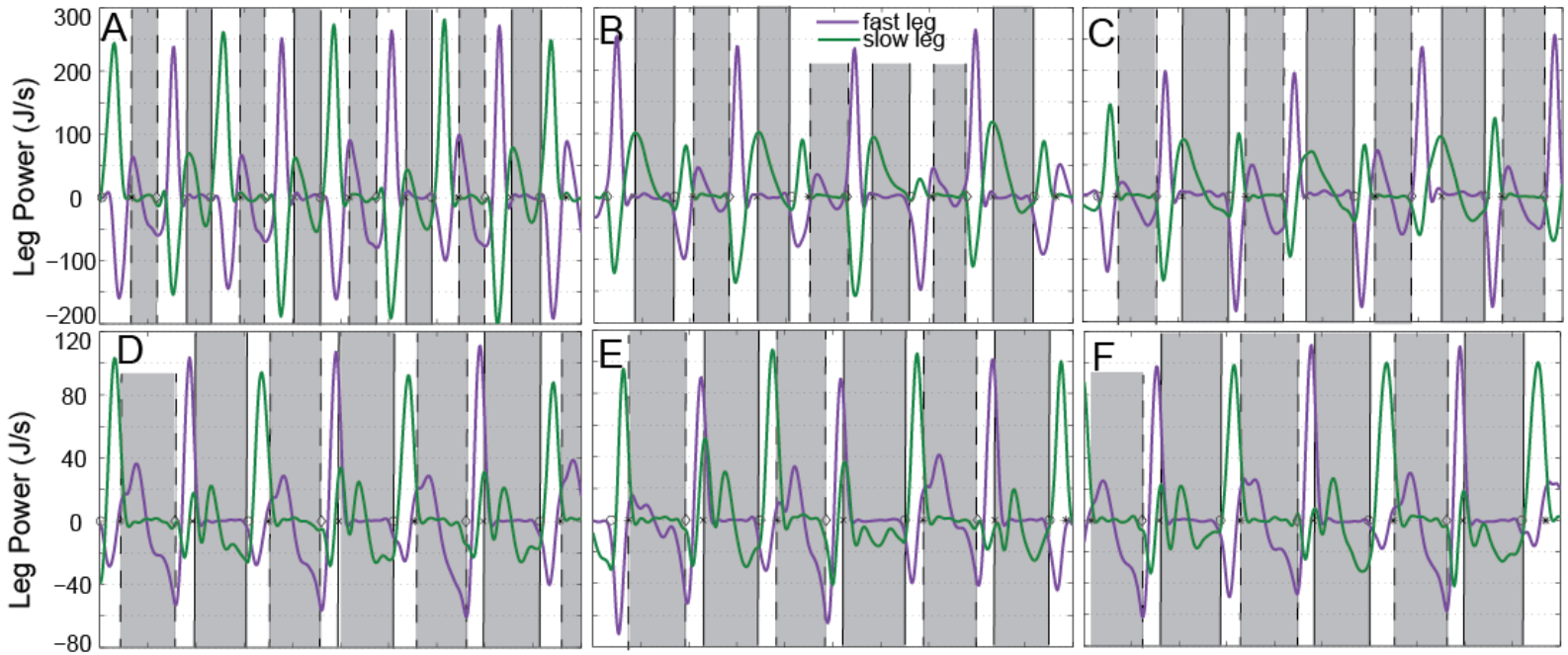

Figure A3.8: Leg power from several strides for a representative amputee subject during fast baseline (A), early adaptation (B), late adaptation (C), slow baseline (D), early post-adaptation (E), and late post-adaptation (F). Slow leg power is green and fast leg power is purple. Pendular phases are shaded gray, with fast leg pendular phase bounded by dashed lines and slow leg pendular phase bounded by solid lines.

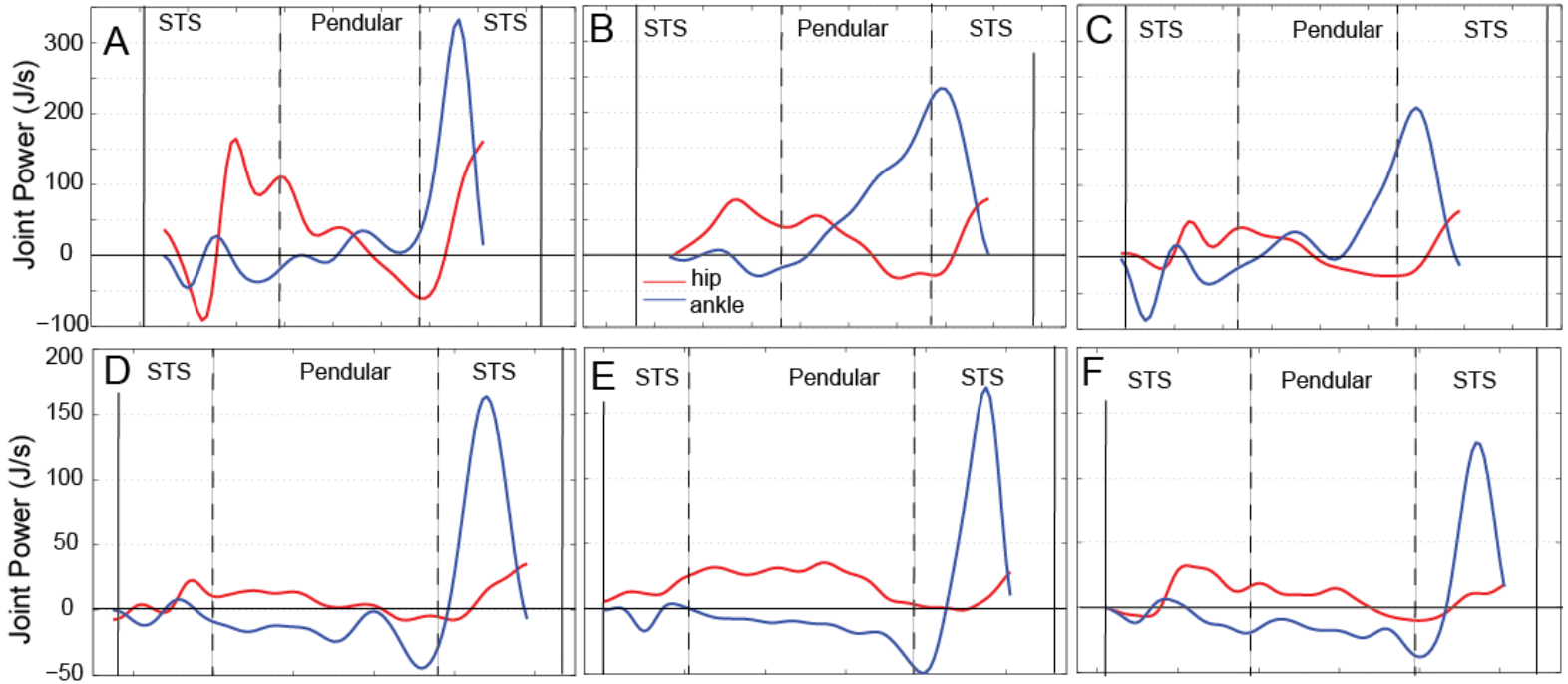

Figure A3.9: Joint power from several strides for a representative control subject's fast leg during fast baseline (A), early adaptation (B), late adaptation (C), slow baseline (D), early post-adaptation (E), and late post-adaptation (F). Hip power is red and ankle power is blue. Fast leg pendular phase bounded by dashed lines.

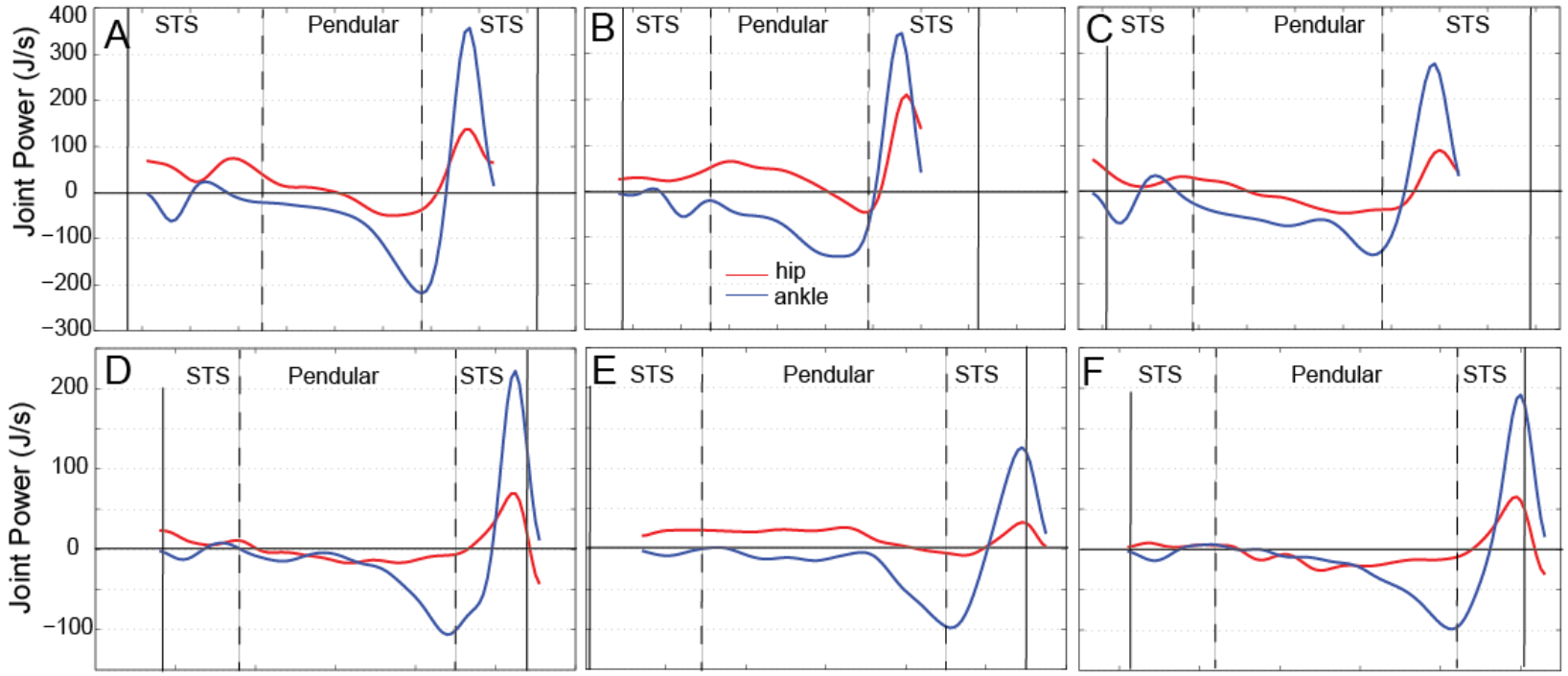

Figure A3.10: Joint power from several strides for a representative amputee subject's fast leg during fast baseline (A), early adaptation (B), late adaptation (C), slow baseline (D), early post-adaptation (E), and late post-adaptation (F). Hip power is red and ankle power is blue. Fast leg pendular phase bounded by dashed lines.

CHAPTER IV

AIM 3: LOCOMOTOR ADAPTATION TO GRADUAL ONSET SPLIT-BELT TREADMILL WALKING IN TRANS-TIBIAL AMPUTEES AND CONTROL SUBJECTS

4.1 Introduction:

An estimated 1.6 million Americans lived with amputation in 2005, and this population is estimated to increase to 3.6 million amputees by 2050 (Ziegler-Graham et al. 2008). Trans-tibial amputation was the second most common type of amputation in the United States, accounting for over 270,000 amputations between 1988 and 1996 alone (Dillingham et al. 2002). In general, transtibial amputees take significantly longer steps with their prosthetic leg leading than with their intact leg leading (Isakov et al. 1997). They also spend more time in stance on their intact leg (Breakey, 1976) and have higher ground reaction force (GRF) on the intact leg (Engsberg et al. 1993; Baker and Hewison, 1990). Trans-tibial amputees also have increased incidence of osteoarthritis on their intact side (Morgenroth, Gelhorn, Suri, 2011; Norvell et al. 2005; Melzer, Yekutiel, Sukenik, 2001).

Because overuse injuries like osteoarthritis are more common on the unaffected side for amputees (Morgenroth et al. 2011; Norvell et al. 2005), and because clinical settings are rarely conducive to measuring kinetics (Childers, Kogler, 2014), improving kinematic asymmetry is a commonly assumed clinical goal (Hassid et al. 1997). Specifically, recent studies have attempted to use split-belt treadmill walking to correct baseline asymmetries in stroke survivors (Reisman et al. 2007, 2009, 2013; Tyrell, Helm, Reisman 2014, 2015) and Parkinson's disease patients (Roemmich et al. 2014a, 2014b). These studies follow the principle of error augmentation, in which the baseline error (i.e.

step length asymmetry) is exacerbated by the split-belt condition. When subjects adapt to the split-belt condition, they correct this error over time. When the split-belt condition is removed, an aftereffect in the opposite direction of the initial asymmetry occurs. If the leg that is leading when subjects take longer steps in baseline is placed on the slow belt during the split-belt condition, the result can be aftereffects that are more symmetric than in baseline or asymmetric in the direction opposite to baseline asymmetry (Tyrell, Helm, Reisman, 2015, Reisman et al. 2007). Although this more symmetric aftereffect would washout after one exposure to split-belt treadmill walking, multiple exposures can lead to a more permanent, newly learned motor pattern (Reisman, Bastian and Morton, 2010). For example, among a group of stroke survivors who performed split-belt treadmill walking 3 times per week for 4 weeks, those with the largest baseline step length asymmetries showed improvements in step length asymmetry that were sustained 3 months later (Reisman et al. 2013). Essentially, the aftereffect was no longer washing out. Therefore, studying the aftereffects of adaptation can provide a glimpse of what may occur in longer term motor learning but can be studied in a timelier, more controlled manner (Reisman, Bastian, Morton, 2010).

In aim 2, I investigated changes in step length symmetry and mechanical work when amputees walked with their prosthesis on the fast belt. This is a useful model for understanding the role of the ankle to locomotor adaptation and the biomechanics of split-belt walking, since it shows us what happens when the ankle is removed. However, because trans-tibial amputees usually take longer steps with the prosthetic leg leading (Isakov et al. 1997), this leg should be on the slow belt during the split-belt condition in order to produce an aftereffect that corrects baseline asymmetry. Therefore, in aim 3, I

tested split-belt walking with the prosthesis on the slow belt to better assess the potential of split-belt walking for clinical use.

To allow successful adaptation to split-belt walking with the prosthesis on the slow belt, it is preferable to gradually speed up the fast belt to twice as fast as the slow belt rather than introducing this split-belt condition suddenly. Amputees spend less time in stance on their prosthetic leg than on their intact leg (Breakey, 1976), likely because they are more comfortable balancing on the intact let. However, sudden onset split-belt walking presents a much greater challenge to both sagittal and frontal plane balance on the slow leg than gradually speeding up the fast belt (Sawers, Hahn, 2013, Sawers et al. 2013). Gradual onset split-belt walking also has better transfer of aftereffects to overground walking (Torres-Oviedo, Bastian, 2012). Since overground walking is more relevant to daily living than treadmill walking, and because gradual onset presents less of a challenge to balance, gradual onset split-belt walking has more potential for clinical use than sudden split-belt walking.

Additionally, while many prior split-belt studies have investigated kinematic asymmetries (Malone, Bastian, 2010; Malone, Bastian, 2014; Malone, Bastian, 2016; Roemmich et al. 2014a; Reisman, Block, Bastian, 2005; Reisman et al. 2013), few have examined kinetic changes in split-belt walking (Roemmich, Stegemoller and Hass, 2012; Ogawa et al. 2014; Mawase et al. 2013; Lauziere S, et al., 2014) and even fewer have examined changes in mechanical work (Thajchayapong et al. in preparation, Roemmich et al. 2014). Amputees produce much less power from their prosthetic ankle than a biological ankle (Bateni, Olney, 2002; Zmitrewicz, Neptune, Sasaki, 2007), but, in order to increase intact leg leading step length, I would expect amputees to increase work from

their amputated leg. Since this work is unlikely to come from the prosthetic ankle, it may come during pendular phase from the hip on the amputated side, which generally does more work in amputees than controls in normal walking (Silverman et al. 2008; Adamczyk, Kuo, 2015). Work from the hip in pendular phase is less efficient than trailing ankle work (Kuo, 2002). In fact, recent work suggests that asymmetry may be unavoidable for amputees to walk efficiently (Adamczyk, Kuo, 2015). Therefore, I calculated joint work and leg work on the CoM in different phases of the gait cycle to determine if work during less efficient phases of gait (i.e. pendular phase) increased when subjects corrected baseline asymmetries.

The purpose of this study was to test whether split-belt treadmill walking would change amputees' baseline inter-leg coordination in post-adaptation. My primary hypothesis was that, if amputees underwent gradual onset split-belt walking with their prosthetic leg on the slow belt, the resulting aftereffect would be opposite the amputees' baseline step length asymmetry. Specifically, I expected amputees to have step length symmetry that was more positive in early post-adaptation than slow baseline. I expected this result, because amputees generally take longer steps with their prosthesis leading, and split-belt treadmill walking results in positive step length symmetry in the aftereffect (Reisman, Block, Bastian, 2005; Roemmich et al. 2014a). This would indicate feedforward control of inter-leg coordination, which would also be supported if there was an aftereffect in double support time. I further hypothesized that both amputees and controls would adapt to gradually introduced split-belt walking by using the same CoM displacement strategy that they used in the sudden onset split-belt walking. Specifically, I expected that, compared to baseline trials, all subjects would move further backward

during fast leg single support and less backward during slow leg single support in late adaptation. Lastly, I hypothesized that, when fast (intact) leg step length increased in early post-adaptation, work in inefficient phases of the gait cycle, such as pendular phase, would increase.

4.2 Methods:

4.2.1 Subjects

Eight trans-tibial amputees (5 male, 76.6k±12.3kg, intact leg length = 88.1±5.9cm) and eight control subjects (5 male, 77.4k±11.3kg, intact leg length = 89.1±6.1cm), who were matched to amputees by gender, leg length and body weight, took part in this study. Control subjects showed no significant differences from amputees in either body mass (mean difference = 0.75kg, $p = 0.60$) or leg length (mean difference = 1.0cm, $p = 0.35$). All subjects gave informed consent in accordance with a protocol approved by the Georgia Institute of Technology Institutional Review Board prior to participating in the study. The cause of amputation was traumatic (7 subjects) or congenital (1 subject), and subjects were excluded if they had limited motion in intact joints or problems with balance. Amputees wore their own, custom-fit prostheses with dynamic response feet. All amputees had their prosthesis for at least 6 months and had their amputation at least 18 months prior to participating in the study. All subjects were able to walk for 15 minutes without additional walking aid.

4.2.2 Experimental Protocol

Because the amputee study participants had differing ability levels, I first determined preferred walking speed (PWS) of each amputee participant. First, I conducted a six-minute walk test (American Thoracic Society, 2002) to determine

participants' overground PWS as an initial estimate of PWS on the treadmill. After allowing participants 2 minutes of acclimation to treadmill walking, I determined PWS by asking them to walk on the treadmill at different speeds. Participants started at 0.9m/s and belt speeds were increased by 0.1-m/s increments. At each speed, the participant had 30 seconds to indicate if the speed was "too fast," "too slow" or "comfortable." If subjects indicated that two consecutive speeds were comfortable, they were asked if the second speed was more comfortable than the first. After increasing to a speed that was deemed "too fast," I repeated the procedure with belt speeds decreasing in 0.1-m/s increments. PWS was determined to be the speed that subjects found comfortable when speeds were both increasing and decreasing. This protocol was similar to a longer, previously used protocol for determining self-selected walking speed (Amorim, Hills and Byrne, 2009). The PWS used for control subjects was that of their matched amputee. Although it is less metabolically costly for able-bodied participants to walk at amputees' PWS (Houdijk et al. 2009), having matched subjects walk at the same speeds allowed for valid comparisons of mechanical work and other variables. Belt speeds for the rest of the experiment were determined based on PWS.

The experimental protocol was initially similar to the protocol of the second aim; subjects completed a baseline trial with both belts moving at 75%PWS (slow baseline 1) followed by a trail with both belts moving at 150%PWS (fast baseline) and a second slow baseline trial (figure 4.1). Subjects also completed an average baseline trial at 112.5%PWS, which was close to PWS and therefore primarily used to determine subjects' initial step length asymmetry. There were two key differences in this experiment: amputees walked with their prosthetic legs on the slow belt, and the fast belt

gradually sped up to 150%PWS from 75%PWS rather than introducing this change in speed suddenly, which would present a greater challenge to balance on the slow leg (Sawers and Hahn, 2013, Sawers et al. 2013). The belt was accelerated at 0.002m/s^2, a rate at which no participants were able to notice the belt accelerating. After the fast belt reached 150%PWS, there was a 3-minute period where both belts moved at a constant speed and a 2:1 belt speed ratio. After resting for 3-5 minutes during which they were not permitted to walk, participants completed a 4-minute trial with both belts moving at 75%PWS. This post-adaptation trial was introduced suddenly to allow for detection of an aftereffect without changing belt speed as a potential confounding factor.

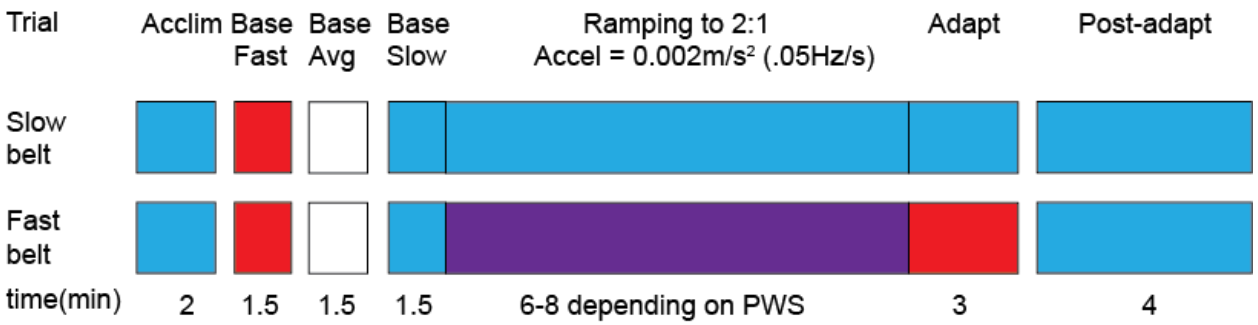

Figure 4.1: Experimental Protocol. Subjects completed a fast baseline trial at 150%PWS (red) and slow baseline trial at 75%PWS (blue). After the second baseline trial, the speed of the fast belt is slowly accelerated (purple) to 150%PWS.

To prevent falls, participants wore a safety harness that did not support body weight for all trials. Also, a mirror in front of the subjects allowed them to see their medial-lateral foot placement. This mirror helped participants avoid stepping on the contralateral belt and stumbling while still maintaining forward gaze.

Control subjects walked with their non-dominant legs on the slow treadmill belt. I determined leg dominance in control subjects by asking them to stand on one leg three separate times during the initial preparations for the experiment. The leg on which they chose to stand was deemed the dominant leg. Previous split-belt walking studies have

used kicking a soccer ball to determine leg dominance (Thajchayapong et al. 2014, Sawers, Hahn, 2013), but I used the one-legged standing task because I was primarily interested in which would be the preferred stance leg during gait. Most tasks used to determine leg dominance (e.g. kicking a soccer ball, picking up a marble) are for determining dominance in skilled movements (Sadeghi et al. 2000; Scheiders et al. 2010), but reaching studies indicates that the limb that is best at skilled movements is not the same as the limb best suited for maintaining stable posture (Shabbott, Sainburg, 2008; Wang, Sainburg, 2007; Sainburg 2005). Furthermore, when I asked amputees to kick a soccer ball, most of them chose to kick the ball with their prosthetic leg. Since I wanted to match the controls as closely as possible to amputees, kicking a ball was not the best way to determine leg dominance. Therefore, the one-legged stance task was better suited for determining leg dominance for split-belt walking.

4.2.3 Data Collection and Processing

I collected data in 2-3 minute increments in all experimental conditions. For the adaptation and post-adaptation conditions, 30 second gaps between each increment allowed for the next trial to be set up in the computer system, which only reliably collected a maximum of 2-3 minutes of data at once. However, I always collected the first 2 minutes and last 30 seconds of belt acceleration and the entire 3-minute period when belts were at a constant 2:1 speed ratio. Similarly, I collected the first 2 minutes and last 90 seconds of post-adaptation. Most of the data that was not collected occurred when one belt was being accelerated. Because the acceleration of the belt made it difficult to tell if changes in work, step length and other variables were due to changing belt speed or changes in motor control, I focused primarily on times when belt speed was not changing

– baseline, post-adaptation and the last 3 minutes of adaptation. I collected kinematic data using a six-camera motion analysis system (120Hz, VICON Motion Systems, Oxford, UK) and retroreflective markers place on the anterior posterior iliac spine, posterior superior iliac spine, greater trochanter, thigh, knee, shank, lateral malleolus, heel and second metatarsophalangeal joint of each leg. For amputees, markers were placed on the prosthesis at the same locations as on the contralateral, intact leg, as has been done previously (Silverman, et al. 2008, Morgenroth, et al. 2011). Therefore, the prosthetic ankle marker placement is not at a true hinge joint, and moments, angular velocities and powers were calculated about a point on the prosthetic foot that had no special significance other than being at the same location on the prosthesis as the ankle was on the intact leg. I collected GRF for each leg with mechanically isolated force plates beneath each treadmill (1080Hz, AMTI, Watertown, MA, USA). I processed marker position and force data with a 4^{th} order Butterworth filter with a 10Hz cutoff frequency.

I made all calculations using custom-written programs written in Matlab (MathWorks, Natick, MA). I calculated joint work, leg work, center of mass displacement and step length symmetry using the same methods as in the second aim. Briefly, I found positive leg work (W^{+})by integrating the dot product of GRF and CoM velocity (v_{com}), using an integration constant based on belt speed (Eq 4.1 and 4.2). Integration constants were determined based on an average vertical CoM velocity of 0 and an average anterior-posterior velocity equal to the belt speed. Similar to aim 2, this gave two separate CoM velocities – one for each belt. During the ramping section of the experiment, I determined the continuously changing speed of the fast belt based on belt acceleration and the time since elapsed since the beginning of ramping. To find joint

work (W_{joint}), I integrated the dot product of joint moment (M_{joint}) and angular joint velocity ($\boldsymbol{\omega}_{joint}$; Eq 4.3). Step length symmetry (SLS) was calculated as the normalized difference between fast-leading and slow-leading step length (SL; Eq 4.4; Reisman, Block and Bastian, 2005), and anterior-posterior CoM displacement (ΔCoM) is the difference between pelvic marker position (in a fixed, laboratory reference frame) at the beginning and end of single support.

$$W^{+} = \int^{+} GRF \cdot v_{com}\, dt \qquad \text{Eq (4.1)}$$

$$W_{loss} = \int^{-} GRF \cdot v_{com} dt \qquad \text{Eq (4.2)}$$

$$W_{joint} = \int^{+} M_{joint} \cdot \omega_{joint}\, dt \qquad \text{Eq (4.3)}$$

$$SLS = (SL_{fast\ leading} - SL_{slow\ leading})/(SL_{fast\ leading} + SL_{slow\ leading}) \qquad \text{Eq (4.4)}$$

To characterize amputees' split-belt adaptation in comparison to previous studies of healthy subjects and other clinical populations, I calculated other temporal variables. I found double support (DS) time when the fast leg was leading (fast-leading DS) and when the slow leg was leading (slow-leading DS; Reisman, Block, Bastian, 2005). This was the difference between the times of leading leg heel strike, when the vertical GRF of that leg exceeded 32N, and trailing leg toe off, when vertical GRF decreased below 32N. I also calculated stance time on each leg as the time between ipsilateral heel strike and toe off.

4.2.4 Statistical Analysis

I performed statistical analyses with Matlab and SPSS (IBM, Armonk, NY, USA), defining late adaptation as the averages of the last 5 steps of adaptation. I defined early and late post-adaptation as the first 5 steps and the last 5 steps of post-adaptation, respectively. To analyze step length symmetry, CoM displacement, DS time, I compared

slow baseline and early and late post-adaptation using repeated measures ANOVA (rmANOVA) followed by post-hoc, pairwise comparisons using Bonferroni corrections. I compared these three trials only because they had identical conditions with both belts moving at 75% PWS. This allowed for a fair comparison that addressed only the hypothesis and was not affected by walking speed, which can by itself alter amputee gait asymmetries (Nolan et al. 2003). For single limb variables (stance time and work variables), I performed 3 rmANOVAs: one compared the fast leg in trials when it moved at 150% PWS (fast baseline, late adaptation), another compared the fast leg when it moved at 75%PWS (second slow baseline, early post-adaptation, late post-adaptation), and the third compared slow leg work in all trials but fast baseline. Note that the rmANOVA comparing the fast leg in fast trials effectively reduces to a paired t-test as it only compares 2 conditions. To determine if subjects had baseline step length asymmetries, I found averages across strides in each trial for every subject, and then compared a vector of the subject averages to zero using Student's t-tests for each baseline trial. All statistical tests had an alpha level of 0.05. P-values below 0.05 indicated significant differences while p-values less than 0.10 but greater than or equal to 0.05 indicated that the difference between two groups approached statistical significance or showed a trend toward significance.

4.3 Results:

Both amputees and controls showed clear aftereffects, taking longer steps with the slow (intact) leg leading than with the fast (prosthetic) leg leading in early post-adaptation. This step length asymmetry in early post-adaptation was significantly different from slow baseline for controls (Figure 4.2A; p=0.002), and amputees (Figure

4.2B; p=0.015). For both groups of subjects, this difference washed out by late post-adaptation, at which point step lengths were significantly more symmetric (closer to 0) than early post-adaptation for both controls (p=0.002) and amputees (p=0.006). If we focus on the pattern of step length symmetry that occurred as the fast belt was accelerating, we see that, for both groups of subjects, step length asymmetry becomes more negative in the first 100 strides but stays relatively constant for the remainder of the adaptation period, even while the belt was still accelerating (Figure 4.2C and D). In the fast baseline trials, amputees average step length asymmetry was significantly less than zero (p=0.0467), with all but one amputee taking longer steps with their prosthetic legs leading. Amputees also had significantly negative step length asymmetry in the average baseline trial (p=0.0326). For amputees' slow baseline trial and all control subjects' baseline trials, step length symmetry was not significantly different than zero.

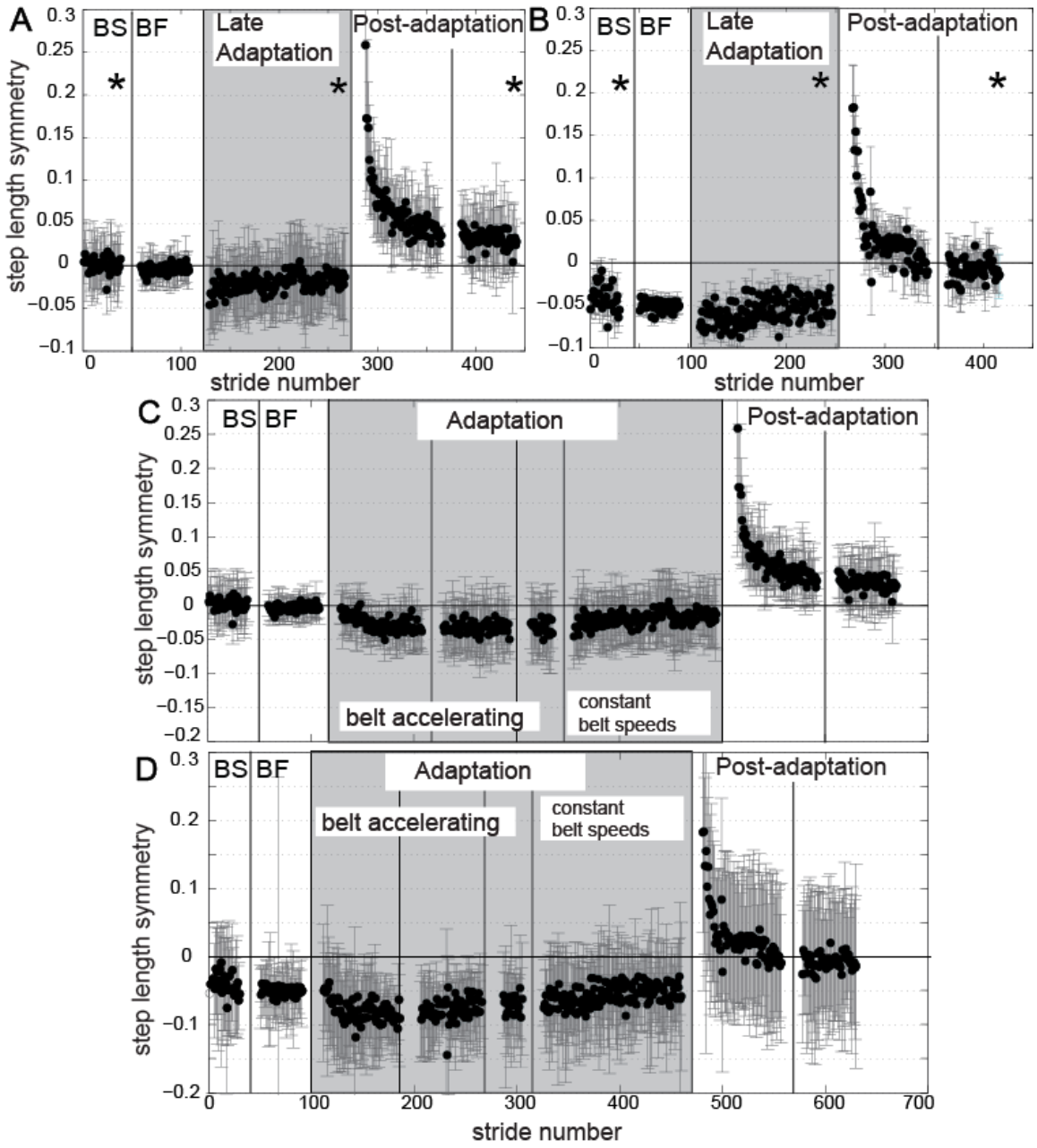

Figure 4.2: Step length symmetry in control subjects (A) and trans-tibial amputees (B). BS and BF are slow baseline (belts at 75% preferred walking speed) and fast baseline (belts at 150% preferred walking speed), respectively. * indicate significant differences from early post-adaptation. In late adaptation, only the constant belt speed portion of adaptation is shown. For descriptive purposes, the full split-belt adaptation trial is shown in control subjects (C) and amputees (D). Error bars denote standard deviation.

In late adaptation, the CoM moved further backwards in a fixed, laboratory reference frame during fast leg single support and further forward during slow leg single

support for both controls and amputees (Figure 4.3). In late adaptation, both controls and amputees moved significantly further forward during slow single support than in slow baseline, early post-adaptation and late post-adaptation ($p<0.03$ for all comparisons). Similarly, all subjects moved further backwards during fast single support in late adaptation than in the fast baseline trial ($p=0.034$ for controls, $p=0.007$ for amputees).

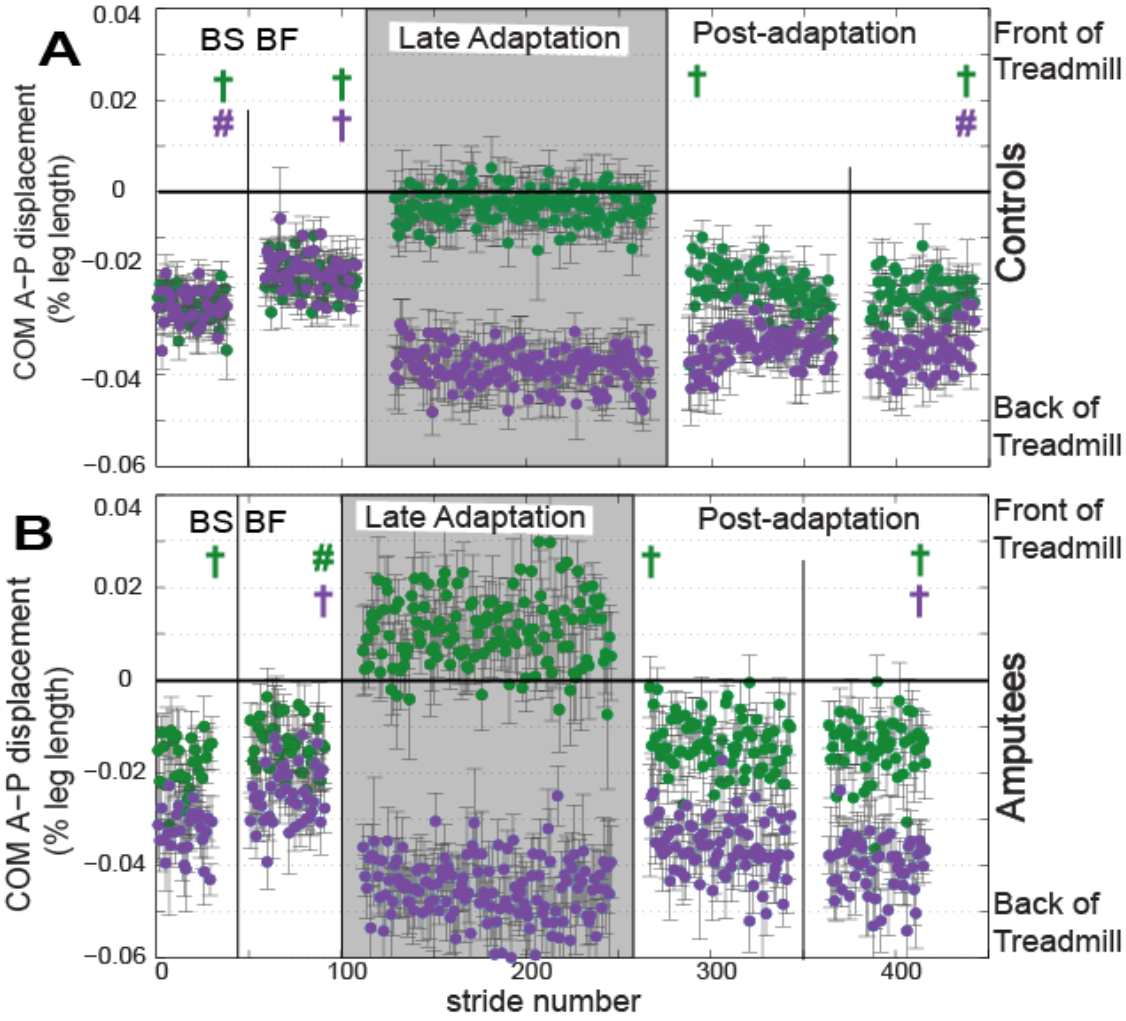

Figure 4.3: Center of mass (CoM) displacement in a fixed reference frame during fast leg single support (purple) and slow leg single support (green) for control subjects (A) and trans-tibial amputees (B). BS and BF are slow and fast baseline trials, respectively. Green and purple † indicate significant differences from late adaptation in CoM displacement during slow single support, while Green and purple # indicate that the difference from late adaptation approached significance for slow single support and fast single support, respectively. Error bars denote standard error. In late adaptation, only the constant belt split-belt speed (2:1 speed ratio between belts) portion of adaptation is shown.

During early post-adaptation, all subjects spent less time in the double support (DS) period when the fast leg was leading (Figure 4.4). Controls had shorter fast-leading double support times in early post-adaptation than in slow baseline ($p<0.001$; Figure 4.4A) and late post-adaptation ($p=0.012$). Amputees also had shorter fast-leading double support times in early post-adaptation than in slow baseline ($p=0.001$; Figure 4.4B) and late post-adaptation ($p=0.008$). For control subjects, slow-leading double support time was significantly greater in early post-adaptation than in slow baseline ($p=0.003$) and late post-adaptation ($p=0.012$) but slow-leading double support time showed no significant differences between trials for amputees (Figure 4.5A and B). In late adaptation, fast (intact) leg stance time was significantly shorter than in fast baseline (data not shown; $p<0.001$ for controls, $p=0.021$ for amputees). Slow (prosthetic) leg stance time was significantly longer in late adaptation than in all other trials ($p\leq0.016$ for controls, $p\leq0.030$ for amputees; Figure 4.6A and B).

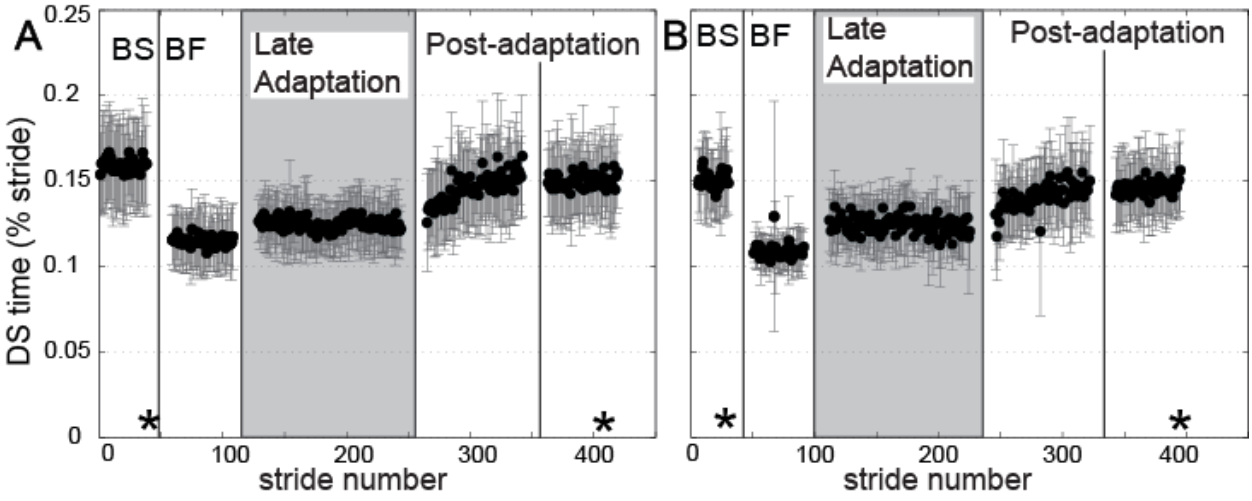

Figure 4.4: Fast leg leading double support time as a percentage of total stride time for control subjects (A) and trans-tibial amputees (B). BS and BF are slow and fast baseline

trials, respectively. * indicate significant differences from early post-adaptation, while # indicates that the difference from early post-adaptation approached significance. Error bars denote standard deviation. In late adaptation, only the constant belt split-belt speed (2:1 speed ratio between belts) portion of adaptation is shown.

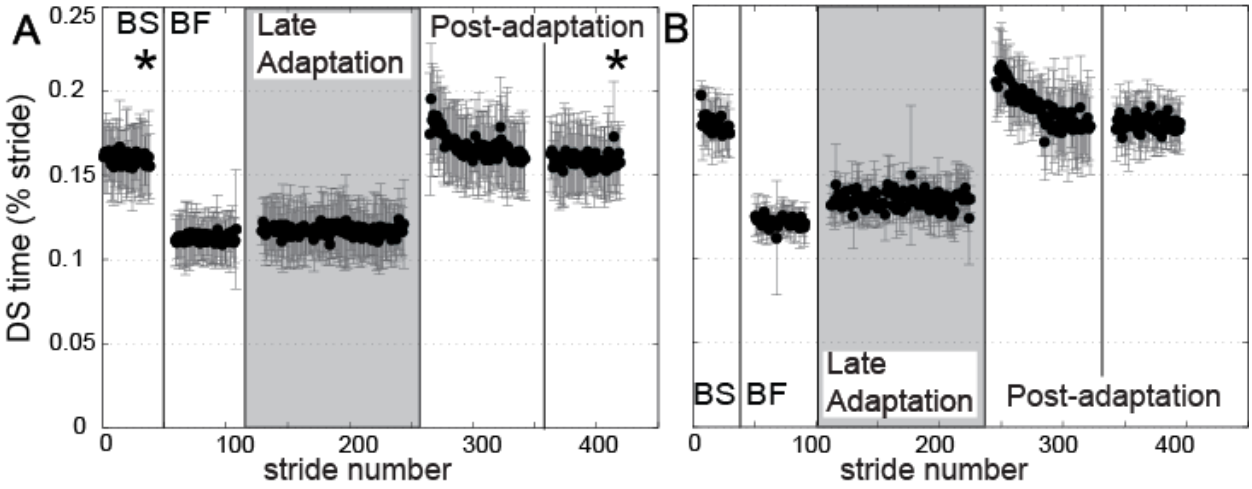

Figure 4.5: Slow leg leading double support time as a percentage of total stride time for control subjects (A) and trans-tibial amputees (B). BS and BF are slow and fast baseline trials, respectively. * indicate significant differences from early post-adaptation. Error bars denote standard deviation. In late adaptation, only the constant split-belt speed (2:1 speed ratio between belts) portion of adaptation is shown.

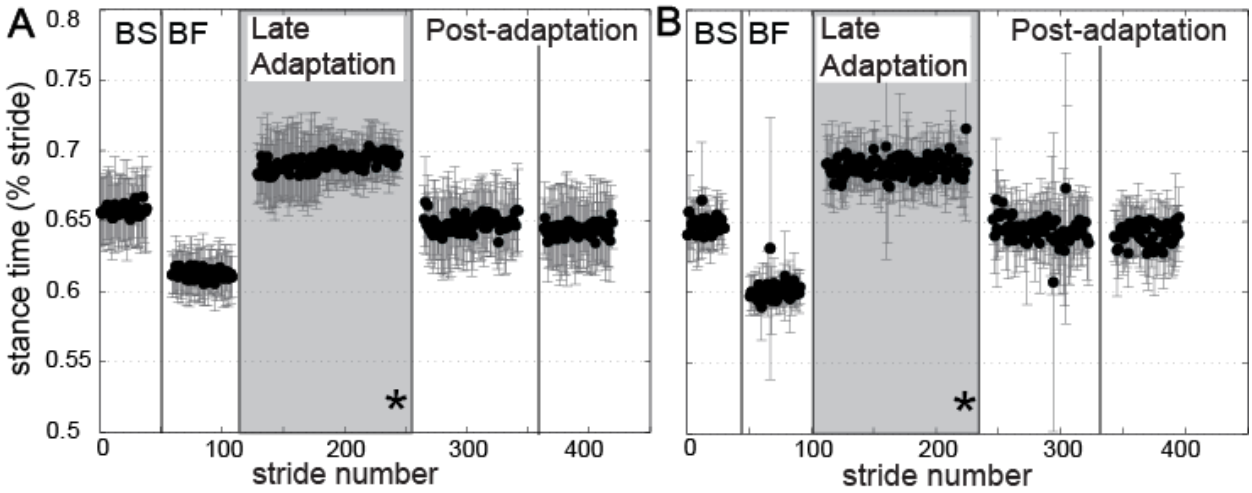

Figure 4.6: Slow (prosthetic) leg stance time as a percentage of total stride time for control subjects (A) and trans-tibial amputees (B). BS and BF are slow and fast baseline trials, respectively. * indicate significant differences from early post-adaptation. Error bars denote standard deviation. In late adaptation, only the constant belt split-belt speed (2:1 speed ratio between belts) portion of adaptation is shown.

Although pendular phase work of the slow leg appears to decrease between early and late post-adaptation for both controls and amputees, there were no statistically significant differences between slow leg pendular work across trials (Figure 4.7). For control subjects, pendular phase work of the slow (prosthetic) leg in early post-adaptation was greater than in slow baseline ($p=0.093$) and late adaptation ($p=0.065$) in a way that approached significance (Figure 4.7A). Pendular work of the fast (intact) leg was significantly less in late adaptation than in fast baseline for amputees ($p<0.001$; Figure A4.1B), but showed no significant differences for controls (Figure A4.1A).

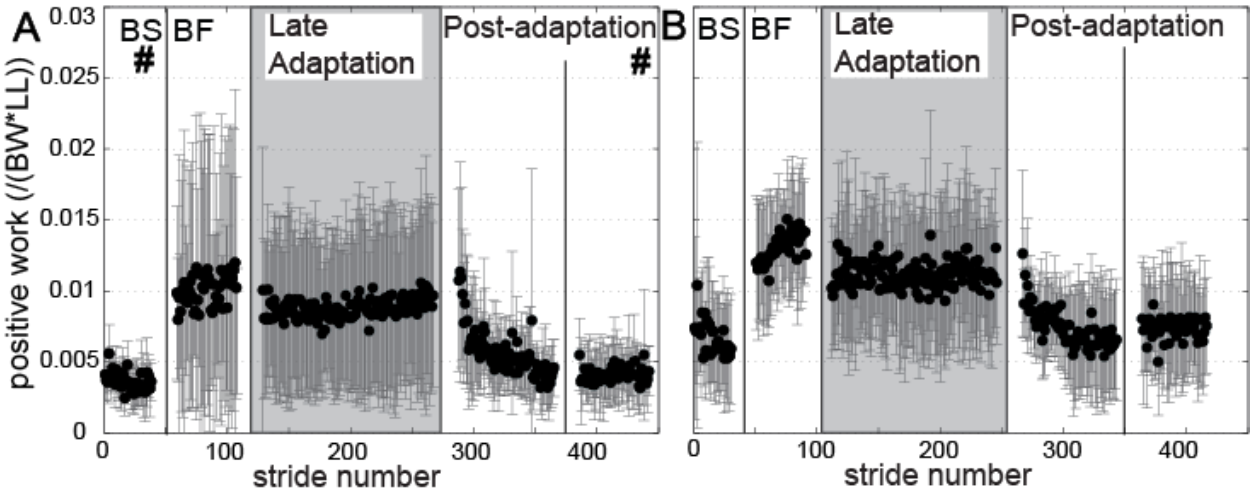

Figure 4.7**:** Slow (prosthetic) leg pendular phase positive work normalized by both body weight and leg length for control subjects (A) and trans-tibial amputees (B). BS and BF are slow and fast baseline trials, respectively. # indicate differences from early post-adaptation that approach significance. Error bars denote standard deviation. In late adaptation, only the constant belt split-belt speed (2:1 speed ratio between belts) portion of adaptation is shown.

Subjects showed few significant changes in positive work done on the CoM and collisional energy loss during STS. There were no significant changes in work done by the slow (prosthetic) trailing leg for either subject, although this work was showed a trend toward being less in early post-adaptation than late post-adaptation for control subjects

(p=0.051; Figure A4.2). Positive work from the fast trailing leg was significantly greater in late post-adaptation than in early post-adaptation for amputees (p=0.011; Figure 4.8B). For controls, positive work from the fast trailing leg was smaller in early post-adaptation than in late post-adaptation (p=0.065) or in slow baseline (p=0.093), but these differences only approached significance (Figure 4.8A). For amputees, collisional energy loss at the fast leading leg was significantly higher in early post-adaptation than slow baseline (p=0.021) and showed a trend toward being higher in early post-adaptation than late post-adaptation (p=0.059; Figure 4.9B). For controls, collisional energy loss at the fast leading leg approached being significantly higher in early post-adaptation than slow baseline (p=0.082; Figure 4.9A). There were no significant differences in collision energy loss from the slow leading leg between trials for either amputees or controls (data not shown).

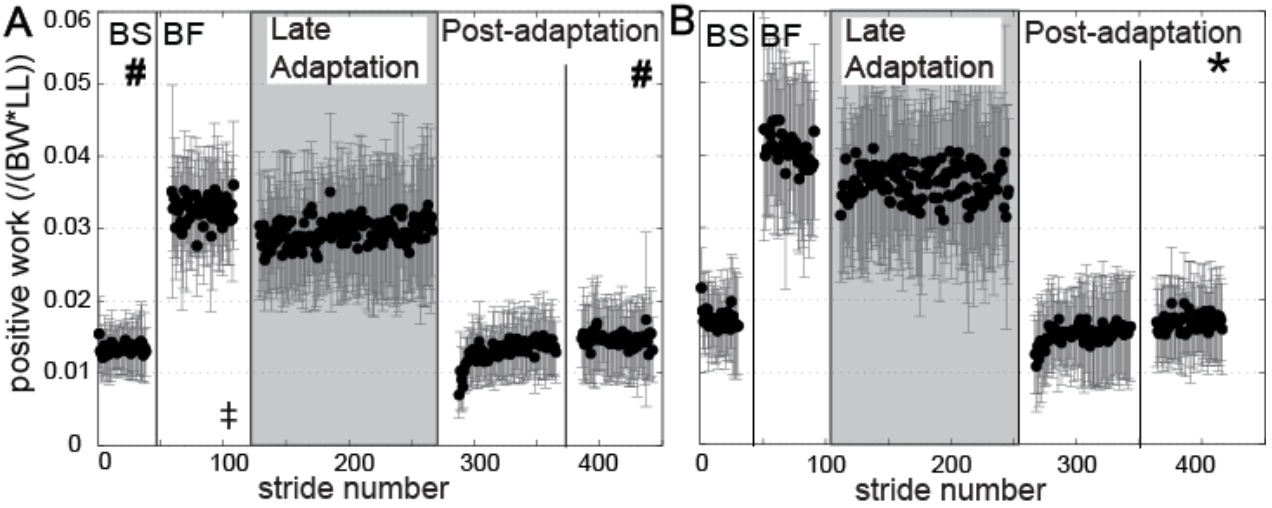

Figure 4.8: Fast (intact) trailing leg positive work during the step-to-step transition, normalized by both body weight and leg length for control subjects (A) and trans-tibial amputees (B). BS and BF are slow and fast baseline trials, respectively. * indicates significant differences from early post-adaptation. # indicate differences from early post-adaptation that approach significance. ‡ indicates a difference from late adaptation that approaches significance. Error bars denote standard deviation. In late adaptation, only the constant belt split-belt speed (2:1 speed ratio between belts) portion of adaptation is shown.

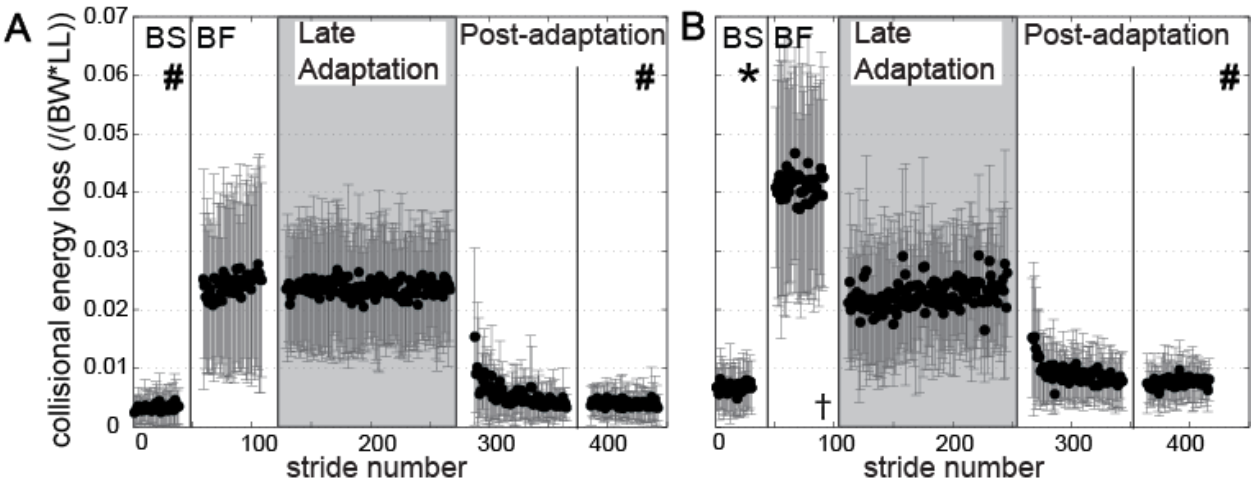

Figure 4.9: Collisional energy loss of the fast (intact) leading leg phase work during the step-to-step transition, normalized by both body weight and leg length for control subjects (A) and trans-tibial amputees (B). BS and BF are slow and fast baseline trials, respectively. # indicate differences from early post-adaptation that approach significance. † indicate significant difference from late adaptation. Error bars denote standard deviation. In late adaptation, only the constant belt split-belt speed (2:1 speed ratio between belts) portion of adaptation is shown.

While fast ankle positive work during stance showed trends toward being lower in early post-adaptation than other trials, positive slow hip work in stance was significantly greater in late adaptation than other trials. Work of the slow hip was significantly greater in late adaptation than early post-adaptation for amputees only ($p=0.035$; Figure A4.3B). Slow hip work was greater in late adaptation than in slow baseline for both controls ($p=0.028$) and amputees ($p=0.003$). The fast hip had significantly greater work in the fast baseline than in late adaptation for controls ($p=0.022$; Figure A4.4B). For amputees, the slow (prosthetic) ankle work significantly increased from early post-adaptation to late post-adaptation ($p=0.027$; Figure 4.10B). Slow ankle work also showed a trend toward

being lower in early post-adaptation than in slow baseline for both controls (p=0.050; Figure 4.10A) and amputees (p=0.077).

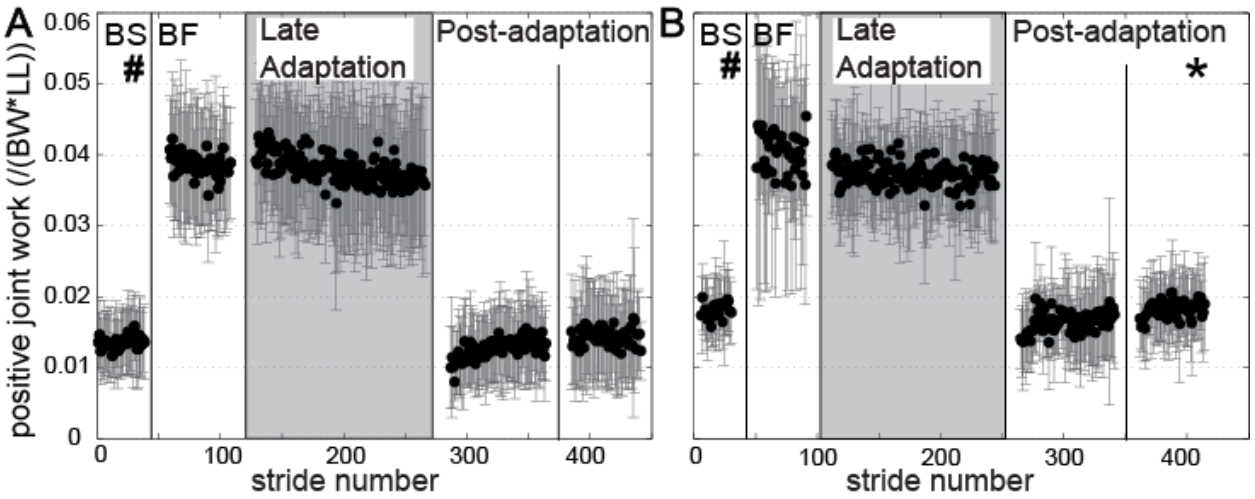

Figure 4.10: Positive work of the ankle on the fast (intact) leg during stance, normalized by both body weight and leg length for control subjects (A) and trans-tibial amputees (B). BS and BF are slow and fast baseline trials, respectively. # indicate differences from early post-adaptation that approach significance. * indicate significant difference from early post-adaptation. Error bars denote standard deviation. In late adaptation, only the constant belt split-belt speed (2:1 speed ratio between belts) portion of adaptation is shown.

4.4 Discussion:

4.4.1 Amputees show adaptation of interlimb coordination similar to that of control subjects

The main hypothesis that the aftereffect in early post-adaptation would oppose amputees' baseline asymmetry was supported. While the primary purpose of this study was to determine if split-belt treadmill walking could result in a correction of amputees' baseline asymmetry in the aftereffect, amputees actually overcorrected their baseline asymmetry, so the aftereffect was even larger than initially expected. In early post-adaptation, amputees took longer steps with the intact leg leading than with the prosthesis leading, and this asymmetry was opposite and larger than amputees' baseline asymmetry

towards taking longer steps with the prosthesis leading. This provides proof of principle that the effects of split-belt treadmill walking can counteract amputees' baseline asymmetry, and is consistent with split-belt walking aftereffects previously found in able-bodied subjects (Reisman, Block, Bastian, 2005; Huynh et al. 2014) and stroke survivors (Reisman et al. 2007; Tyrell, Helm, Reisman, 2015). The aftereffect and subsequent, gradual de-adaptation back to step length symmetry indicate that amputees, like healthy subjects, use feedforward control of step length symmetry. Rather than correcting the asymmetry in early adaptation in a reactive manner based on immediate sensory feedback, subjects used predictive control, which was updated slowly over many strides, to determine their step lengths. Thus, upon immediate removal of the split-belt condition, subjects had a large error in step length symmetry because their motor control system was still predicting that the belts were moving at different speeds.

Amputees did not have particularly large slow baseline step length asymmetries in the current study, which could have contributed to overshooting symmetry in de-adaptation. While amputee step lengths were not significantly asymmetric in the slow baseline trial, they were significantly asymmetric in fast and average baseline trials. Step lengths were shortest overall in the slow baseline trial, and it is possible that walking at 75%PWS did not challenge push-off from the prosthetic trailing leg enough to create significantly shorter step lengths when the intact leg was leading (Silverman et al. 2008). Because the average baseline trial had the speed closest to preferred walking speed (112.5%PWS), and because most subjects took longer steps with the prosthetic leg in all baseline trials (6 of 8 subjects in slow and average baseline, 7 of 8 subjects in fast baseline), it is reasonable to conclude that the subject group had a negative step length

asymmetry overall. While trans-tibial amputees generally take longer steps with the prosthetic leg leading, it should be noted that not all trans-tibial amputees share this asymmetry (Hansen et al. 2006). Step length asymmetry varies based on rollover shape of the prosthetic foot (Hansen et al. 2006) and is also likely affected by the amputee's rehabilitation time and overall fitness. Future split-belt walking studies should screen subjects for baseline step length asymmetry and either exclude those who walk with longer intact leading steps or put their intact limb on the slow belt during the split-belt condition.

Both control subjects and amputees demonstrated a typical aftereffect fast leg leading double support time. Both groups spent significantly less time in fast leading double support during early post-adaptation than during late post-adaptation or slow baseline. This indicates feedforward control and is consistent with previous findings in healthy subjects of an aftereffect in double support ratio (slow leading double support time/fast leading double support time; Reisman, Block, Bastian, 2005). Control subjects spent more time in double support with the slow leg leading during early post-adaptation than during late post-adaptation or the slow baseline trial. Amputees had the same pattern of longer slow leading double support time in early post-adaptation, but this difference was not significant. It is possible that the lack of significance results from using only a 2:1 belt speed ratio. Reisman and colleagues found that aftereffects in double support time were not as strong with a 2:1 ratio as with higher belt speed ratios (2005), but 2:1 belt speed ratios are generally used in studies with clinical populations that are incapable of larger ranges of walking speeds (Reisman et al. 2009; Roemmich et al. 2014a; Roemmich et al. 2014b). Step length symmetry and double limb support times are both

interlimb variables, and the aftereffect observed in both of these variables suggests that subjects use feedforward control for adaptation of interlimb coordination. This study is the first to show that trans-tibial amputees also exhibit these aftereffects, which indicate feedforward interlimb adaptation. This finding suggests that feedforward control of interlimb coordination is not affected by limb loss.

Neither amputees nor controls exhibited an aftereffect in slow (prosthetic) leg stance time. Both groups had slow leg stance times that were significantly different in late adaptation than in baseline, but stance time went immediately back to slow baseline levels in post-adaptation, indicating that stance time is controlled reactively based on sensory feedback. This is also consistent with prior studies of healthy individuals (Reisman, Block, Bastian, 2005). However, given that amputees have compromised feedback from the amputated leg during stance, reactive control of stance time must not be reliant on feedback from the foot or stretch receptors like Golgi tendon organs or spindles in the tibialis anterior or triceps surae, which no longer relate to motion or torque of the amputated ankle. Rather, amputees are likely using sensory feedback from proximal muscles and joints. This does not necessarily mean that feedback from stretch receptors in the tibialis anterior or triceps surae is not involved in reactive control of stance time in control subjects. All amputees in this study had their amputations over 1 year ago. Given the plasticity of the nervous system, amputees may have had long-term changes in how they process sensory feedback such that they do not use sensory feedback from the same joints as controls to regulate stance time.

4.4.2 Center of mass displacement strategy is a robust response to split-belt condition

CoM displacement results support the hypothesis that subjects would move backward in fast leg single support and forward in slow single support during late adaptation. As in chapter 3, subjects move backwards during fast single support, likely saving energy by walking slower than the fast belt at a speed that is closer to PWS. To avoid moving off of the back of the treadmill, they make up for this backward movement with increased forward movement in slow single support. This meant that they were moving at a faster speed than the slow belt, which also put them closer to PWS. CoM displacement is likely an energy-saving strategy, because amputees and healthy controls walk more efficiently as they walk at slower speeds (Cavagna, Kaneko, 1977; Gonzalez, Corcoran, Reyes, 1974, Waters et al. 1988). Due to the changing belt speed in early adaptation, this experiment cannot determine if the change in CoM displacement was a gradual or immediate response to the split-belt condition, but the results from chapter 3 indicate that it is a gradual response for controls. Although this strategy had not been shown in split-belt walking previously, the CoM displacement strategy is a consistent response to the split-belt walking condition. Control subjects and amputees employ this strategy whether the split-belt condition is introduced suddenly or gradually. Amputees employ this strategy if the prosthesis is on the fast belt as in chapter 3, but they even employ the CoM displacement strategy when the prosthesis is on the slow belt. The preference to move forward on the slow belt in late adaptation was stronger than amputees' tendency to rely on their intact leg more than their amputated leg. Even when it required them to move backwards when on their sound, intact leg and move forward in single support on their prosthesis, amputees still used the CoM displacement strategy.

An interesting result was that there was no significant aftereffect in CoM displacement during single support. If CoM displacement resulted from true, feedforward adaptation, as the gradual change in control subjects' CoM displacement in chapter 3 suggests, we would expect to see an aftereffect when the split-belt condition was removed. In the tied belt condition experienced in post-adaptation, both belts are moving at the same speed so there is no energetic benefit to the CoM displacement strategy. Given that aftereffects often dissipate more quickly than the initial adaptation (Selgrade and Chang 2015, Davidson and Wolpert 2004; Malone, Bastian, 2010; Bastian 2008), it could be that, without any energetic benefit to the CoM displacement strategy, it dissipated too quickly to be detected by averaging the first 5 strides of post-adaptation. Subjects quickly went back to their baseline behavior, which was likely not fully "un-learned" during the split-belt adaptation trial. However, it is difficult to see even a non-significant change CoM displacement during single support between baseline and early post-adaptation, and this difference was far from even approaching significance for any subjects in either fast or slow single support ($p>0.20$). It may be less appropriate to think of single support CoM displacement, which represents whole body movement during one portion of the gait cycle, simply as a result of feedback control or feedforward control. Movements of many different body parts affect CoM displacement in single support, and some of these movements may be under feedforward control while some are controlled reactively via sensory feedback.

4.4.3 Work data suggest that split-belt walking induces no improvement in efficiency during post-adaptation

There were few clear changes in leg work on the CoM for either subject group, so the data do not allow for clear conclusions. One clear aftereffect did occur: amputees'

fast (intact) leg collisional energy loss is significantly higher in early post-adaptation than slow baseline ($p=0.021$). Additionally, the difference between early and late-post adaptation approaches significance for amputees ($p=0.059$). These results indicate that amputees increased collisional energy lost by the fast leg in the aftereffect using feedforward control. Such an increase would hurt mechanical efficiency in constant speed, tied belt walking, because positive work should be increased to make up for the energy lost (Ruina, Bertram, Srinivasan, 2005). Otherwise, the subject could not maintain his position on the treadmill. Since positive trailing leg work is more efficient than work in other points in the gait cycle (Kuo, 2002), if it were highest in early post-adaptation, the detriment to mechanical efficiency would be minimal, but this is not the case. Positive work of the fast (intact) trailing leg actually significantly increased from early to late post-adaptation, although neither significantly differed from slow baseline. Similarly, ankle work in stance significantly increased from early to late post-adaptation, which is consistent with the increase in trailing leg work because most positive ankle work is done when the leg is trailing (Perry, Burnfield, 2010; Neptune, Kautz, Zajac, 2001). The only phase of the gait cycle when positive work appeared higher in early post-adaptation than in slow baseline was slow (prosthetic) leg work during pendular phase, but this difference was not significant for either amputees or controls. Therefore, I cannot conclude with any certainty that the mechanical work done in early post-adaptation increased during this less efficient phase of gait, so the third hypothesis was not supported.

It is more reasonable to conclude that, in early post-adaptation, there was no changes in work that increase in positive work during STS and no decrease in positive work during pendular phase. It is curious however, that there were significant changes in

step lengths and CoM displacement but no corresponding significant changes in work. I suspect that work had higher variability between subjects and, therefore, the changes in work that led to these kinematic changes were simply not statistically significant. Changes in work were not large enough to achieve significance but may have been large enough to move a subject significantly further forward on the slow belt.

4.4.4 Clinical implications

It is unsurprising that amputees overshot step length symmetry in the aftereffect, as this overshoot has also been shown in stroke survivors after split-belt walking (Malone and Bastian 2014; Tyrell, Helm, Reisman, 2015).Using a belt speed ratio less than 2:1 would be more likely to result in symmetric step lengths in the aftereffect (Lauziere et al. 2014). Stroke survivors who had symmetric step length symmetry aftereffects were less likely to de-adapt (Tyrell, Helm, Reisman, 2015), so the same effect may be seen in amputees. If that were the case, a split-belt intervention designed to correct step length asymmetry on a long-term basis would be more likely to be successful if the initial aftereffect were symmetric.

Another benefit of using a smaller belt speed ratio is that it would allow amputees to walk at their preferred walking speed in post-adaptation. Because amputees have a lower preferred range of walking speeds than controls (Giest, Chang, 2016), I had to use a slow speed of 75%PWS to achieve a 2:1 ratio. This meant that, in post-adaptation, subjects were moving at a speed slower than their comfortable walking speed. While this study demonstrates that split-belt treadmill walking can correct step length asymmetry, it would be more relevant to daily life to correct step length asymmetry at amputees' typical walking speeds.

4.4.5 Limitations and future studies

The major limitation of this work is that I did not test changes in amputees' metabolic power, which is the most direct way to determine physiological energetic cost. We know that control subjects reduce metabolic cost as they adapt to split-belt walking, but we have no information about how amputees' metabolic power changes. One drawback of measuring metabolic power via gas exchange is that this method takes minutes to assess metabolic power, meaning that, compared to mechanical work, it has poorer temporal resolution. Still, without metabolic power data, I can only make conclusions about mechanical efficiency rather than physiological energy costs. I have partially addressed this issue by focusing on changes in work done by joints known to have different efficiencies and in phases of the gait cycle with different efficiencies, but my analysis cannot capture every change in efficiency that affects metabolic cost. For example, a change in joint power can be achieved through passive dynamics of elastic structures such as the Achilles tendon, or through concentric muscle contractions that require more energy (Biewener, Roberts, 2000). Using electromyography to determine changes in muscle activity could also shed light on whether mechanical changes are primarily due to active or passive musculoskeletal actions.

Metabolic power collection via gas exchange and electromyography were omitted from the current study for two related reasons. First, given the lack of previous work in this area and anecdotal evidence that some amputees had difficulty with split-belt walking with the prosthesis on the slow belt, it was initially unclear that amputees would be able to complete the split-belt protocol with the prosthetic leg on the slow belt. These concerns turned out to be unfounded, as most amputees reported very little trouble with the gradual onset split-belt protocol, but it was not possible to know this with certainty

until after amputees had done the experiment. Considering that preparation for metabolic power and EMG measurements would add time to the experiment, it would have made it more difficult to recruit amputee subjects that were already scarce given the study's inclusion criteria. Now that we know trans-tibial amputees can accomplish the split-belt walking task with their prosthesis on the slow belt, future studies should investigate how amputees' metabolic power and muscle activity change during adaptation to split-belt walking and subsequent de-adaptation.

Future studies should also investigate how adaptation of step length symmetry transfers to overground walking in amputees. Prior work shows that, in able-bodied subjects, compared to sudden onset split-belt walking, gradual introduction of the split-belt condition results in better overground transfer of learning, indicated by larger aftereffects in step length symmetry (Torres-Oviedo, Bastian, 2012). This improvement in overground transfer likely occurs because gradual split-belt walking restricts errors in symmetry to their natural range, making subjects less likely to associate their motor learning with only the context of treadmill walking. Better overground transfer is a potential benefit of split-belt treadmill walking, because overground walking is more closely related to activities of daily living than treadmill walking is.

4.5 Conclusion

In summary, amputees respond to gradual onset split-belt walking with kinematic adaptation patterns similar to those of control subjects. They both show step length symmetry aftereffects in early post-adaptation and use the CoM displacement strategy in late adaptation. Despite these kinematic changes, there were very few significant changes in leg work and joint work between trials. However, the kinematic adaptations indicate

that amputees use feedforward control to change their interlimb coordination in response to split-belt treadmill adaptation.

A4 Appendix: Additional Mechanical Work Figures

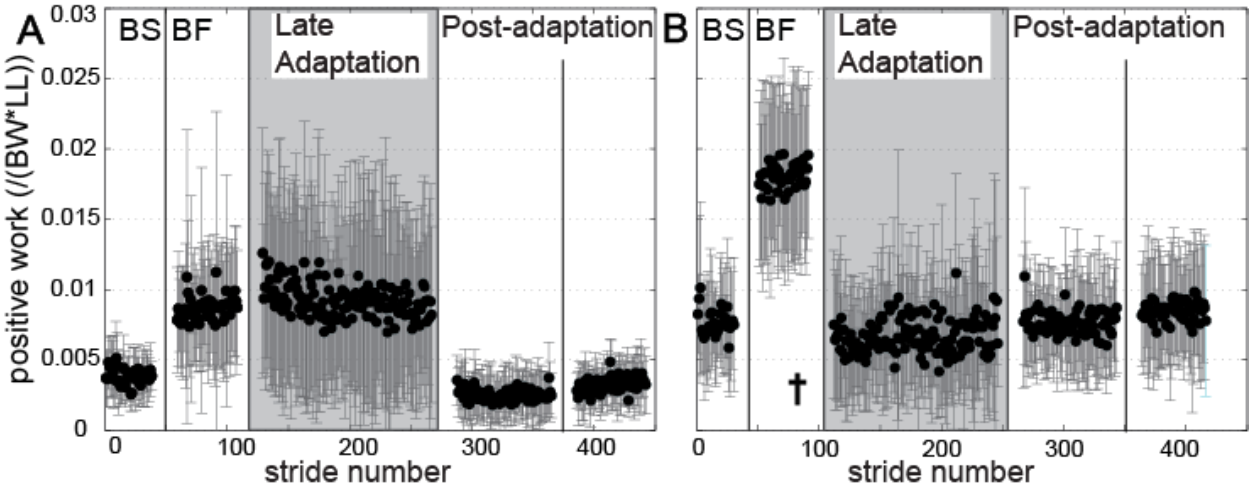

Figure A4.1: Fast (intact) leg pendular phase positive work normalized by both body weight and leg length for control subjects (A) and trans-tibial amputees (B). BS and BF are slow and fast baseline trials, respectively. † indicate significant difference from late adaptation. Error bars denote standard deviation. In late adaptation, only the constant belt split-belt speed (2:1 speed ratio between belts) portion of adaptation is shown.

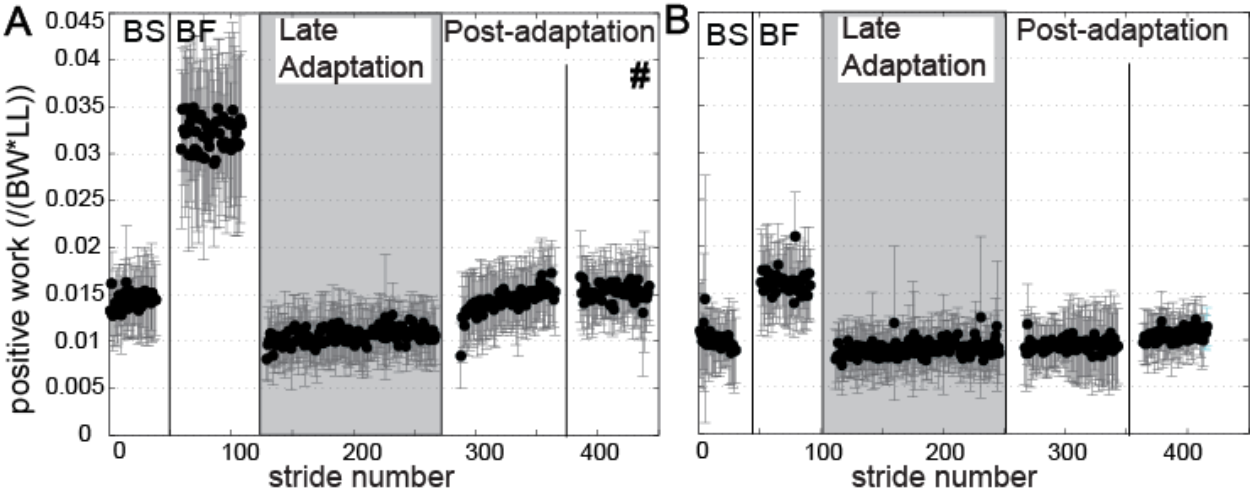

Figure A4.2: Slow (prosthetic) trailing leg phase positive work during the step-to-step transition, normalized by both body weight and leg length for control subjects (A) and trans-tibial amputees (B). BS and BF are slow and fast baseline trials, respectively. # indicate differences from early post-adaptation that approach significance. Error bars denote standard deviation. In late adaptation, only the constant belt split-belt speed (2:1 speed ratio between belts) portion of adaptation is shown.

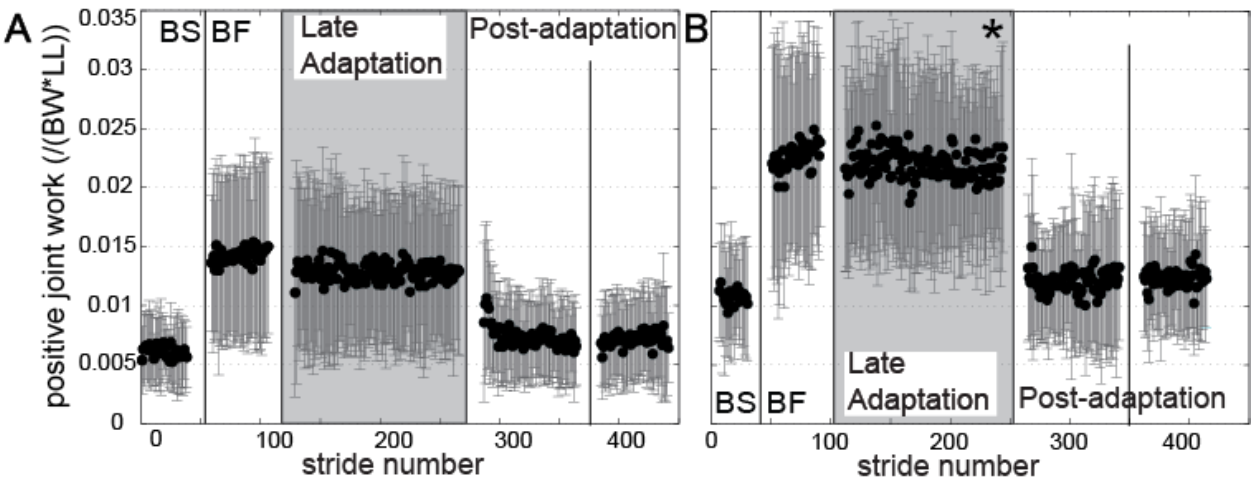

Figure A4.3: Positive work of the hip on the slow (prosthetic) leg during stance, normalized by both body weight and leg length for control subjects (A) and trans-tibial amputees (B). BS and BF are slow and fast baseline trials, respectively. * indicate significant difference from early post-adaptation. Error bars denote standard deviation. In late adaptation, only the constant belt split-belt speed (2:1 speed ratio between belts) portion of adaptation is shown.

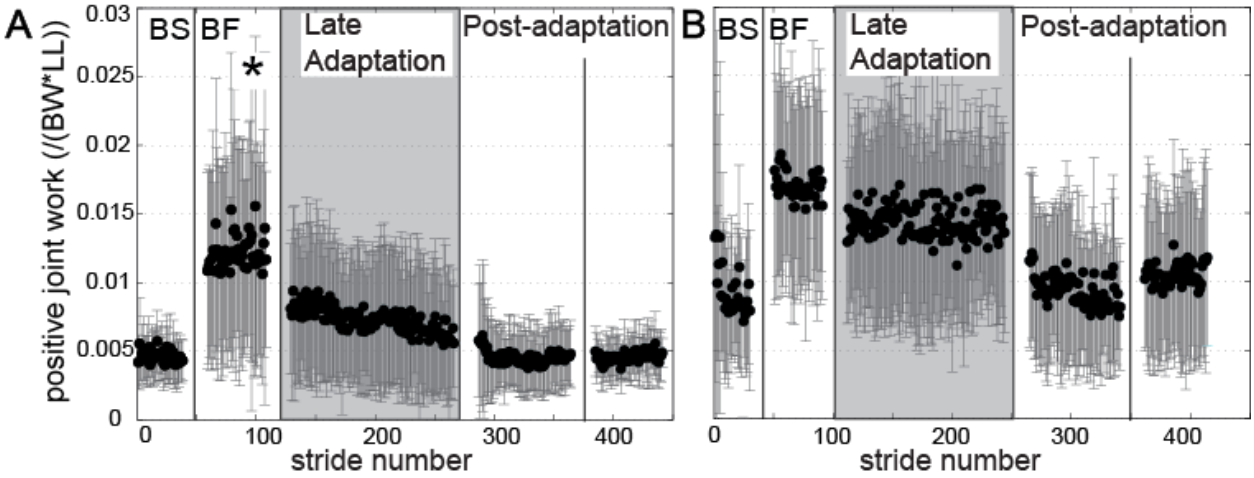

Figure A4.4: Positive work of the hip on the fast (intact) leg during stance, normalized by both body weight and leg length for control subjects (A) and trans-tibial amputees (B). BS and BF are slow and fast baseline trials, respectively. † indicate significant difference from late adaptation. Error bars denote standard deviation. In late adaptation, only the constant belt split-belt speed (2:1 speed ratio between belts) portion of adaptation is shown.

CHAPTER V

CONCLUSIONS

Given the number of different environments in which humans walk, locomotor adaptation is an important part of daily life. Determining changes at the joint and leg level during locomotor adaptation helps us better understand how the nervous system changes coordination of these elements to adapt to new environments. Studying adaptation can also give us a glimpse of what to expect in long-term learning.

5.1 Major findings

In Aim 1, I investigated task-relevant and task-irrelevant deviations in joint torques during hopping as subjects adapted to visual feedback. My hypothesis that subjects would preferentially reduce task-relevant deviations in accordance with minimal intervention principle was supported for the part of the experiment when subjects were reducing errors in GRF. However, once subjects were no longer improving but only maintaining GRF, they reduced all deviations equally, regardless of relevance to the GRF task. I conclude that during limb force adaptation, subjects switched from a minimal intervention strategy during performance improvement to a noise reduction strategy during performance maintenance, which may represent a general coordination strategy for locomotor adaptation of limb force in other bouncing gaits, such as running.

In Aim 2, my primary goal was to analyze coordination of joint work during split-belt treadmill walking adaptation in control subjects and trans-tibial amputees. I found that control subjects adapted by reducing hip work as they adjusted their ankle work timing such that work from the trailing ankle in STS increased. Because work from the

ankle in STS is more efficient than work from the hip, this ankle timing strategy is a possible mechanism for the reduction in metabolic power during split-belt walking adaptation. Additionally, all subjects increased collisional energy loss as they adapted but did not increase leg work to compensate for this. Instead, as they adapted, all subjects began moving further backward on the fast belt. This CoM displacement strategy is another possible energy-saving strategy, because it allows subjects to walk slower than the fast belt speed. The only difference between amputees and controls was that amputees began moving further forward on the slow belt more quickly than controls, possibly because this was the only compensation available to the amputees, whose prostheses were on the fast belt.

In Aim 3, I tested inter-leg coordination and mechanical work in gradual onset split-belt treadmill walking, which allowed trans-tibial amputees to walk with the prosthesis on the slow belt. I found significant aftereffects in step length symmetry and double support time, indicating that inter-leg coordination was adapted using feedforward control. Alternatively, there was no aftereffect in stance time for either group, indicating feedback control, even for the amputated leg. Both amputees and controls used the CoM displacement strategy, with controls and amputees moving backwards on the fast belt and compensating on the slow belt, even though the prosthesis was on the slow belt. Despite these kinematic changes, there were few significant changes in mechanical work. Amputees did significantly increase collisional energy loss in early post-adaptation, but this was not accompanied by any changes in positive work from baseline.

5.2 Implications – Biomechanics of split-belt walking adaptation

One surprising finding in aim 2 was that net work – collisional energy loss subtracted from the sum of all positive work terms – does not have to stay constant at zero for split-belt walking with both belts at constant, different speeds. Collisional energy loss by the fast leading leg in STS increases significantly for all subjects during split-belt adaptation, which is to be expected in some ways, because collisional energy loss only increases to fast baseline levels. However, an increase in collisional energy loss hurts efficiency in normal walking b/c it must be made up for by propulsive work to maintain constant average speed (Kuo, Donelan Ruina, 2005; Donelan, Bertram, Srinivasan, 2005). In split-belt walking, subjects don't do this. They allow backwards movement on the fast belt but compensate by limiting backward motion on slow belt. They make up for the net negative work in fast-leg-leading STS with a net positive work in slow-leg-leading STS, but, because fast leg and slow leg work occur in different reference frames, there is not a one-to-one relationship between work needed to maintain on the slow belt and work needed to maintain position on the fast belt. Therefore, as subjects adapt to split-belt walking and learn to go backwards, they have a significant decrease in net work performed on the CoM. This result underscores that split-belt walking is a very different mechanical circumstance than overground or even tied belt walking. Therefore, even when each belt in the split-belt condition moves at a constant speed, assumptions that can normally be made for constant speed walking, such as zero net work, no longer apply.

The ankle timing strategy revealed in aim 2 also helps to resolve an apparent contradiction between prior studies. Thajchayapong et al. showed that fast trailing leg work increased as healthy subjects adapted to split-belt walking (in preparation), but

Finley, Bastian and Gottschall did the same experiment and found that gastrocnemius activity decreased over the same time course (2013). Given that the triceps surae are the primary muscle powering work done by the trailing leg (Neptune, Kautz, Zajac, 2001), one might expect gastrocnemius EMG to increase with increasing trailing leg work. The results of aim 2 indicate that subjects actually decrease ankle work in stance, which corresponds with reduced gastrocnemius EMG, but shift their timing such that ankle work in stance is concentrated in STS. This suggests that fast trailing leg work is increased by concentrating ankle work and, presumably, gastrocnemius activity, in STS rather than increasing ankle work and gastrocnemius activity over all of stance.

5.3 Implications – Motor control

5.3.1 Minimal intervention in hopping adaptation

The switch in control strategies from minimal intervention to noise reduction occurs during practice of activities as diverse as finger force generation (Latash et al. 2003) and leg force in hopping (Selgrade, Chang, 2015), suggesting that it is the result of a centralized control strategy. The cerebellum is essential to locomotor adaptation during novel walking tasks (Morton et al. 2006, Jayaram et al. 2011) and drives adaptation by using sensory errors to update the forward model of the motor task (Tseng et al. 2007). Changes in motor-evoked potentials elicited by transcranial magnetic stimulation during human gait adaptation also suggest corticospinal tract involvement in human gait adaptation (Barthelemy et al. 2012). During cat locomotion, the motor cortex and corticospinal tract modify muscle synergies resulting in altered interjoint coordination during visually guided stepping over obstacles (Drew et al. 2008). Further evidence suggests that sensorimotor control of movement is organized hierarchically (Loeb et

al.1999), with fewer, task-relevant parameters being represented at higher levels of the nervous system, and a larger number of neuromuscular degrees of freedom (e.g. individual motor units, muscles and joints) at the lower levels of the nervous system. Likewise, it is possible that centrally mediated pathways are involved in controlling and altering the interjoint coordination strategy I observed during limb force adaptation in hopping subjects and in split-belt walking. Future work is necessary to investigate how coordination strategies at the muscle level affect kinetic adaptations during locomotion.

5.3.2 Feedforward control of inter-leg parameters in split-belt adaptation

Aftereffects in aim 3 generally supported that inter-leg parameters are controlled in a feedforward manner and stance time is controlled through feedback alone. Interestingly, cat split-belt walking does not demonstrate the gradual changes in EMG or kinematics (Frigon, Thibaudier, Hurteau, 2015) that are indicative of feedforward adaptation in human split-belt adaptation (Reisman, Block, Bastian, 2005; Finley, Bastian, Gottschall, 2013). This discrepancy may be related to the significant mechanical differences between quadrupedal, digitigrade cat walking and human walking. Feedforward adaptation may be unique to bipedal split-belt walking, which has single support phases in which balance is challenged (Sawers et al. 2013; Sawers, Hahn, 2013). Recent work shows that humans increase fore-aft margin of stability on the fast belt as they adapt to split-belt walking (Finley, Park, 2015), so it may be that the purpose driving feedforward adaptation is to improve balance. Alternatively, reducing metabolic cost could be driving adaptation as previously suggested (Finley, Bastian, Gottschall, 2013), and the mechanical factors that adapt such as decreasing hip work, and pendular phase

work and increasing trailing ankle and leg work (Thajchayapong et al, in preparation) provide more energetic benefit for bipedal, plantigrade walking.

While this research did not focus on neuroanatomy, I can make inferences about the structures in the central nervous system involved in feedforward adaptation based on previous literature. The cerebellum is a key component in feedforward adaptation, as patients with cerebellar lesions are unable to adapt to tasks such as split-belt treadmill walking (Morton, Bastian, 2006), throwing with visuomotor perturbation (Martin et al. 1996) and reaching in force fields (Maschke et al. 2004). Specifically, adaptation may be mediated partly by long-term depression in Purkinje cells of the cerebellum. This process occurs during motor learning in monkeys and involves an increase in complex spikes – high frequency bursts of action potentials with small amplitude – in Purkinje cells, causing changes in cerebellar plasticity and depressing single action potentials (Medina, Lisberger, 2008). The relationship between long-term depression of single action potentials in Purkinje cells and adaptation is also supported by a reduction of cerebellar inhibition during split-belt walking adaptation in humans (Jayaram et al. 2011). It is therefore likely that changes at the cerebellar level were essential to adaptation to the sudden onset split-belt condition in chapter 3.

However, the cerebellum may play less of a role in adaptation to the gradual onset split-belt condition in chapter 4. Patients with severe cerebellar ataxia were better able to correct reaching errors in a force field when the field was introduced gradually than when it was introduced abruptly (Criscimagna-Hemminger, Bastian, Shadmehr, 2010). On the other hand, in both gradual and sudden onset of the force field, cerebellar patients did not overcompensate for the force field early in the reaching movement, meaning they did not

adapt in the most optimal manner (Izawa et al. 2008). Optimal control (i.e. maximizing performance of accurately hitting a target while minimizing costs like energy expended or a correlate of energy such as force) is a theory with broad applications in motor learning (that can also explain the lack of changes in task-irrelevant deviations in early adaptation in the hopping study in chapter 2 (Todorov, Jordan, 2002; Todorov, 2004). Reducing task-irrelevant deviations presumably requires expending energy, but task-irrelevant deviations have no impact on performance by definition. Based on the role of the cerebellum in reaching adaptation to split-belt walking, I could speculate that the cerebellum is at least partially responsible for not only the improvement in step length symmetry in sudden onset split-belt walking, but also for the increase in ankle work during STS and decrease in hip work, which improve mechanical efficiency. However, reaching and gait are distinct tasks that should not be assumed to have the same control mechanisms, so further study would be necessary to test this speculation.

The biological benefit to adaptation is generally thought to be a reduction of effort and metabolic cost. This is supported by studies of adaptation in reaching (Izawa et al. 2008; Huang, Ahmed 2014) and gait (Emken et al. 2007; Finley, Bastian, Gottschall, 2013), which show that metabolic cost and effort decrease as subjects adapt to new environments. In these studies, effort is typically measured by cost functions that include force, muscle activations, coactivation, or other variables that can be generally classified as proxies for energy expended. Unlike typical reaching adaptation studies, and unlike the hopping adaptation study in chapter 2, split-belt treadmill adaptation has no explicit goal of matching or reaching a target. Rather, step length symmetry is generally used as an error measurement in split-belt studies, with symmetric step lengths (symmetry = 0)

assumed to correspond with zero error. However, while step length symmetry and metabolic power decrease in the same general time frame (Finley, Bastian, Gottschall, 2013), it is not clear that kinematic symmetry in gait leads to the lowest energetic costs. Symmetric step times in tied belt walking do result in lower metabolic bower during tied belt treadmill walking (Ellis, Howard, Kram, 2013). However, when reaching in a force field, subjects adapt to reach in a way that is optimal but does not return to the straight line trajectory seen in baseline trials before the field is applied (Izawa et al. 2008). Therefore, we should not assume that people walking on a split-belt treadmill will always have the same kinematic symmetry in late adaptation as in tied belt conditions, nor should we assume that kinematic symmetry is energetically optimal in the split-belt condition. Perhaps the reason why control subjects overshot symmetric step lengths during split-belt adaptation in chapter 2, and in previous literature (Vazquez et al. 2015), is that slight asymmetries in step lengths may result in no energetic penalty in the split-belt condition. It is especially important to avoid assuming that kinematic symmetry is optimal in clinical populations with unilateral impairments, such as amputees who can only produce efficient ankle work during STS with one leg.

5.3.3 Optimal feedback control in explicit and implicit locomotor adaptation

By viewing the chapter 2 hopping study through the lens of optimal feedback control, we can better understand the switch from locomotor control consistent with minimal intervention in early adaptation to total noise reduction in late adaptation. The experimenter, by instructing study participants to match the visual force target, created an explicit task for the subjects to follow. This likely caused minimization of task error to be weighted very heavily in the cost function that controlled the subjects' hopping. For this

reason, subjects first only reduced joint torque deviations that affected task error. Once task error was minimized, they began reducing all joint torque deviations regardless of task relevance. This suggests that there were other terms in the cost function not related to the task. Perhaps decreasing task-irrelevant deviations in joint torques optimized another variable such as muscle activity or allowed the subject to adopt a leg posture that used less energy to meet high force hopping demands. Due to the nature of the experiment, it is difficult to say with any certainty what the other terms to be optimized in the cost function are, but previous work suggests that, during locomotion, the motor control system minimizes energy or related variables like muscle activation (Emken et al. 2007).

In contrast, the task to which subjects adapt in split-belt treadmill walking is implicit. Unlike reaching for a target or the chapter 2 hopping study, there is no explicit target or goal defined by the experimenter, who only instructed subjects to walk with one foot on each treadmill belt. Minimal intervention may have played a role, but the study participants had multiple implicit goals which are not known with certainty. I suspect that none of these goals were prioritized in a cost function as highly as the explicit task of matching hopping force to a target in chapter 2. Reduction of expended energy is likely to be an implicit goal based on reduced metabolic power in previous adaptation studies (Finley, Bastian, Gottschall, 2013; Huang, Ahmed, 2012; Huang, Ahmed, 2014). One possible implicit goal may be maintaining constant velocity, which appears to be the case in constant-speed, tied-belt treadmill walking (Dingwell, Cusumano, 2010), presumably to avoid moving off of the back of the treadmill. While constant velocity is difficult if not impossible when one belt moves twice as fast as the other, subjects may be using the

center of mass displacement strategy to bring their velocities on each belt closer together in an effort to avoid moving off the back of the treadmill. This may have been the closest subjects could come to maintaining constant velocity given the instructions to walk with one foot on each belt. If not for these instructions, subjects could have walked solely on the slow belt in the split-belt condition, saving energy and maintaining constant velocity. Future work should use cost functions to explore how people optimally adapt their motor control to split-belt walking.

5.3.4 Feedback control of stance time in split-belt adaptation

Another particularly interesting result was that stance time on the slow (prosthetic) leg had no aftereffects, indicating that humans control stance time through sensory feedback, even when distal proprioceptive feedback from the foot and ankle is compromised. This result suggests that proprioceptive feedback from more proximal joints is responsible for initiating the transition from stance to swing phase. In spinal cats, transition from stance to swing occurs at 80-90 degrees of hip extension due feedback from hip muscles and joint afferents (Grillner, Rossignol, 1978; Kiehn 2006). My results could suggest that humans may use similar hip proprioception to transition from stance to swing phase, although further study would be necessary to conclude this with certainty.

5.4 Clinical implications

This dissertation has potential applications to clinical research using split-belt treadmill walking and visual feedback as potential therapies. Visual feedback of step length and stance time has been used to alter kinematic symmetry in healthy subjects and amputees, with effects generally similar to those of split-belt walking (Kim, Krebs, 2012; Dingwell, Davis, Frazier, 1996). Visual feedback of GRF symmetry can also improve

GRF symmetry in amputees and hip replacement patients (Dingwell, Davis, Frazier, 1996; White, Lifeso, 2005), while visual feedback of impact peak or related quantities like tibial acceleration can also lower peak impact force in distance runners, potentially reducing risk of tibial stress fracture (Agresta, Brown, 2015; Crowell, Davis, 2011; Crowell et al. 2010; Clansey et al. 2014). Visual feedback for potential clinical use typically focuses on a single joint or limb-level parameter such as GRF, but may cause unintended consequences at other joints. UCM analysis, and particularly the modified UCM analysis first presented in aim 1, could provide a way to analyze coordination of joints to achieve a limb-level goal such as a change in GRF, and could be employed with visual feedback experiments in running and walking with only minor changes. This would result in a better understanding of how the nervous system changes coordination as we adapt to specific visual feedback protocols with clinical potential, rather than only elucidating a gross result (e.g. lower impact GRF).

The lack of an aftereffect in CoM displacement in aim 3 did not prevent there from being an aftereffect in step length symmetry, suggesting there is not a strong link between these two variables. In a prior study of amputee gait, Roerdink and colleagues showed that step length symmetry was not adequate to fully describe asymmetry in overground prosthetic gait (2012). Rather, step length symmetry can be broken up into trunk progression asymmetry and forward foot placement asymmetry. CoM displacement in treadmill walking is analogous to trunk progression, so rapid or immediate de-adaptation of CoM displacement could be related to why stroke survivors do not maintain a more symmetric step length aftereffect after an intervention involving repeated split-belt exposure (Reisman et al. 2013). If this were the case, limiting patients'

use of CoM displacement could affect how quickly aftereffects washout or how well they are maintained after repeated split-belt exposure.

A drawback of gradually introduced split-belt walking is that it does not produce savings as strongly as sudden onset split-belt walking (Torres-Oviedo, Bastian, 2012; Roemmich, Bastian, 2015). In other words, when subjects experienced a split-belt condition days after the initial split-belt exposure, those who initially completed sudden onset split-belt walking adapted more quickly to the second exposure. This would be problematic in designing a long-term, gradual split-belt therapy, which involves repeated split-belt exposures over the course of several weeks and works best if subjects have less to relearn in the repeated split-belt exposures. Studies of reaching adaptation indicate that random variations in task can result in better savings than gradual onset perturbations (Turnham, Braun, Wolpert, 2012; Herzfeld et al. 2014). Models supported by evidence from reaching, stance and split-belt adaptation suggest that an aftereffect in the same direction as a subsequent perturbation can cause savings, even if the aftereffect resulted from an initial adaptation to the opposite perturbation (Herzfeld et al. 2014; Malone, Vasudevan, Bastian, 2011; Sarwary, Selen, Medendorp, 2013). Therefore, future long-term studies could benefit from exposing subjects to an initial bout of split-belt therapy that reduces baseline step length asymmetry in the split-belt condition followed by gradual, error augmentation split-belt training, which reduces step length asymmetry in the aftereffect. I would expect the aftereffect caused by the initial split-belt exposure to result better savings in the subsequent error augmentation exposure(s), and gradual error augmentation has the most potential for reducing step length symmetry in overground walking (Roemmich, Bastian, 2015; Torres-Oviedo, Bastian, 2012).

However, it is also important to avoid assuming that producing more symmetric gait after split-belt adaptation is a desirable clinical outcome overall. Kinematic asymmetry is often an assumed goal clinically, presumably because it is relatively easy to observe (Childers, Kogler, 2014; Hassid et al. 1997), and it certainly has the benefit of improved cosmesis for patients who walk to walk more normally compared to their able-bodied peers. Better cosmesis could lead to a more active lifestyle that would benefit overall health, especially for vascular amputees, who make up the majority of amputees (Varma, Stineman, Dillingham, 2014). Therefore, cosmesis should not be dismissed as a benefit.

However, the argument that amputees should improve step length symmetry, because those with asymmetric step lengths have higher incidence of intact side overuse injuries is based only on this correlation and has no causal link. Osteoarthritis could be linked to any of trans-tibial amputees' other asymmetries, such as stance time asymmetry (Breakey, 1976), which is feedback-controlled and thus not corrected by split-belt walking, or GRF asymmetry (Baker, Hewison, 1990; Silverman et al. 2008). Given that osteoarthritis is a degenerative disease that develops over years, it is difficult to prove that any of these asymmetries causes osteoarthritis, but knee adductor moment and loading rate in the intact leg has been shown to be strongly associated with knee osteoarthritis in trans-tibial amputees (Morgenroth et al. 2011; Morgenroth, Gelhorn, Suri, 2012). Therefore, future work should use inverse dynamics to assess frontal plane moments and loading rates in amputees after split-belt walking adaptation. Given that subjects generally have higher fast leg braking forces in the aftereffect (Ogawa et al. 2014) and amputees had higher intact leg collisional energy loss in the aftereffect (aim 3),

it is possible that increased forces could increase knee moments, which could make osteoarthritis more likely.

Walking with symmetric step lengths could also hurt clinical populations in terms of energetic efficiency. Split-belt walking does nothing to improve trailing prosthetic leg work in the aftereffect, and Adamczyk and Kuo argue that, with this deficiency, trans-tibial amputees have to walk asymmetrically to be most efficient (2015). Therefore, using a powered prosthesis that restores trailing leg work may be a preferable treatment for amputees (Herr, Grabowski, 2012). Future work should determine if trailing leg or ankle work increase in the post-split-belt aftereffect for stroke survivors. If not, they may have the same problem with inefficiency in symmetric walking. In early post-adaptation, intact leg positive STS work appeared to be lower and slow leg pendular phase work appeared to be higher compared to baseline (aim 3). However, these results were not significant and also occurred when step length was asymmetric towards the intact leg taking longer steps, so it is unclear from our results whether work would be done in more or less efficient phases of gait if step length were symmetric. Future split-belt studies should use smaller belt speed ratios to achieve symmetric aftereffects and analyze joint and leg work in different phases of the gait cycle to determine if split-belt walking affects efficiency in post-adaptation walking.

5.5 Limitations and Future Studies

A major limitation of this dissertation is that I did not test changes in metabolic power. One drawback of measuring metabolic power via gas exchange is that, compared to mechanical work, it has poorer temporal resolution. Thus, measuring metabolic cost using VO_2 would not be appropriate for an experiment with short trials, such as in aim 1.

Still, without metabolic power data, I can make conclusions about mechanical efficiency, which is related to metabolic cost (Donelan, Kram, Kuo, 2002; Wutzke, Sawicki, Lewek, 2012), but cannot make direct conclusions about physiological energy costs. This is less problematic for control subjects, since previous work indicates that their metabolic power decreases during split-belt adaptation, but there are no data on metabolic cost in amputees during split-belt walking. Now that trans-tibial amputees have shown they can accomplish the split-belt walking task with their prosthesis on the slow belt, future studies should investigate how amputees' change metabolic power during adaptation to split-belt walking and subsequent de-adaptation.

Another limitation specific to the second aim was the use of the handrail by all subjects in the first 30 seconds of each trial. This affected the anterior-posterior GRF of several of the subjects, some of whom pushed forward on the handrail, resulting in greater GRF, and some of whom produced less GRF, presumably because they pulled on the handrail to maintain forward position. Therefore, this data had to be disregarded. Since the largest changes occur in early adaptation and early de-adaptation, the variables that did show significant changes from early to late adaptation in aim 2 must have been particularly robust. Based on previous work (Thajchayapong et al. in preparation), I suspect that changes in positive trailing leg work and positive pendular phase work over the course of adaptation would have been significant as well had subjects not used the handrail. The handrail was especially detrimental to detecting aftereffects, which washout at faster rates than adaptation (Malone, Bastian, 2010; Bastian 2008; Selgrade, Chang 2015). This is supported by the aftereffects in by the gradual onset experiment in aim 3, which likely had similar aftereffects to what aim 2 would have had without the

handrail (Roemmich, Bastian, 2015; Torres-Oviedo, Bastian, 2012). In figures 4.2, 4.4, 4.5A, 4.8, 4.9 and 4.10, there is either a significant aftereffect or significant washout, but the aftereffect largely dissipated after 30 strides of post-adaptation. I recommend that future studies of amputee split-belt walking eschew anterior handrail use for subject safety in favor of a safety harness. With some clinical populations, using a handrail is unavoidable (e.g. Roemmich et al. 2014). In these cases, I suggest minimizing the time spent holding the rails to the first 5-10 seconds of each trial if possible. Alternatively, if subjects regularly walk using canes or walkers, these devices could be used in the study and instrumented with strain gauges and use force to quantify clinical subjects' reliance on such assistive devices.

Future studies measuring EMG and in conjunction with metabolic power to quantify changes in muscle activity as amputees adapt to split-belt walking would also be interesting. Previous work in intact subjects shows that integrated EMG of the gastrocnemius and tibialis anterior are more strongly correlated with metabolic power than other muscles (Finley, Bastian, Gottschall, 2013). In amputees, these muscles are not functional on one leg, so it would be interesting to see if missing these muscles caused proximal, ipsilateral, leg muscles to more strongly correlate with metabolic power or just strengthened the correlation between contralateral, intact ankle muscles and metabolic power. Additionally, measuring muscle activity during split-belt walking would give a more direct measure of changes in the amputees' nervous system during locomotor adaptation.

5.6 Final thoughts

The purpose of this dissertation was to investigate changes in inter-limb and inter-joint coordination during locomotor adaptation in healthy subjects and trans-tibial amputees. The results presented here shed more light on how changes in coordination of joint work relate to improved efficiency during split-belt adaptation and also show that split-belt walking adaptation has the potential to correct amputees' baseline step length asymmetries. However, there is still much to be learned about causes changes in mechanical work changes after split-belt adaptation, not only in amputees, but also in other clinical populations. Studies of error augmentation therapy focus primarily on step length symmetry but should, in the future, also focus on kinetic variables, particularly mechanical work in different phases of gait. This will give us a better idea of whether or not aftereffects of split-belt walking could improve the walking ability and overall health of patients with gait asymmetries.

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VITA

BRIAN P SELGRADE

Brian Selgrade was born in North Carolina and grew up in Raleigh. He graduated from North Carolina State University with a B.S. in Biology in 2007. He then spent a year as an Americorps VISTA in Nashville TN, establishing a summer reading program for low-income children and conducting research on the effectiveness of volunteer readers in public schools. He joined the Comparative Neuromechanics Lab at Georgia Tech in 2011 after completing his master's thesis on fluid dynamics in a ventricular assist device. When he is not working, he enjoys spending time with his wife Liz, his dog Elsie, and his daughter Maggie, who is the world's cutest baby.